106663533

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(FILE 'HOME' ENTERED AT 19:02:26 ON 05 APR 2004)

FILE 'MEDLINE' ENTERED AT 19:02:35 ON 05 APR 2004

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L1          283 S 5HT1A
L2         4308 S HT1A
L3         4537 S L1 OR L2
L4            8 S L3 AND OBESITY
L5         2604 S L3 AND ANTAGONIST?
L6            8 S L4 AND OBESITY
L7            0 S L6 NOT L4
L8         2117 S L3 (P) ANTAGONIST?
L9            4 S L8 AND OBESITY
L10          33 S L8 AND EATING
L11          32 S L10 NOT L9
L12           0 S L11 AND DIORDER?
L13           3 S L11 AND DISORDER?
L14         359 S L2 (W) ANTAGONIST?
L15          18 S L1 (W) ANTAGONIST?
L16         377 S L14 OR L15
L17           2 S L16 AND OBESITY
L18           3 S L16 AND EATING
L19           0 S L16 AND FLUSHING
L20           1 S L16 AND ADDICTION
L21           6 S L16 AND SEXUAL
L22           3 S L3 AND VASOMOTOR
L23          46 S L8 AND REVIEW?
L24           2 S L16 AND REVIEW?
L25           2 S L24 NOT L17
L26          44 S L23 NOT L25
L27          44 S L26 NOT L4
L28          44 S L27 NOT L6
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106663533

=> d 1-8 bib abs

L4 ANSWER 1 OF 8 MEDLINE on STN
AN 2001644973 MEDLINE
DN PubMed ID: 11697445
TI Investigations on possible serotonergic involvement in effects of OB-200G (polyherbal preparation) on food intake in female mice.
AU Kaur G; Kulkarni S K
CS Pharmacology Division, Univ Inst Pharm Sci, Panjab University, Chandigarh, India.
SO European journal of nutrition, (2001 Jun) 40 (3) 127-33.
Journal code: 100888704. ISSN: 1436-6207.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011108
Last Updated on STN: 20020123
Entered Medline: 20011205
AB BACKGROUND: OB-200G is a polyherbal preparation containing aqueous extracts of Garcinia cambogia, Gymnema sylvestre, Zingiber officinale, Piper longum and resin from Commiphora mukul, all possessing thermogenic properties. Our previous studies reveal OB-200G to exert antiobesity effects in dietary animal models of **obesity**. AIM OF THE STUDY: The present study investigated the possible involvement of serotonergic system in the effect of OB-200G on food intake. We examined the effects of systemic pretreatment with 5-HT depletor, p-chlorophenylalanine (PCPA, 300 mg/kg, i. p. for 6 days), 5-**HT1A** agonist, (8-hydroxy-2-(di-N-propylamino)-tetralin (8-OH-DPAT, 0.1 mg/kg, i. p.), nonselective 5-HT antagonist, cyproheptadine (1 mg/kg, i. p.), 5-HT2 receptor antagonist, seganserin (1 and 2 mg/kg, i. p.) and 2-deoxy-D-glucose (2-DG, glucose antimetabolite, 500 mg/kg, i. p.) on satiety induced by OB-200G (500 mg/kg, p. o.) in non-deprived female mice. The results were compared with fluoxetine (10 mg/kg, i. p.), a selective serotonin reuptake inhibitor. METHODS: Fifteen minutes after the last drug administration, groups of mice were presented with sweetened chow and the amount of food consumed was recorded at 0.5,1,2, 3 and 4h time intervals. RESULTS: The hyperphagic effect of PCPA, 8-OH-DPAT, cyproheptadine and 2-DG was significantly ($p < 0.05$) antagonized by both OB-200G and fluoxetine. However, the anorectic effect of fluoxetine was not reversed by centrally acting 5-HT2 antagonist, seganserin but the latter markedly attenuated the satiety action of OB-200G. CONCLUSION: The present observations suggest the role of serotonin in mediation of satiety by OB-200G and hence its antiobesity effect.

L4 ANSWER 2 OF 8 MEDLINE on STN
AN 2001088284 MEDLINE
DN PubMed ID: 10928397
TI Olanzapine-induced glucose dysregulation.
AU Bettinger T L; Mendelson S C; Dorson P G; Crismon M L
CS College of Pharmacy, University of Texas at Austin, and Texas Department of Mental Health and Mental Retardation, 78712, USA.
SO Annals of pharmacotherapy, (2000 Jul-Aug) 34 (7-8) 865-7.
Journal code: 9203131. ISSN: 1060-0280.
CY United States
DT (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200101
ED Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010112
AB OBJECTIVE: To report a patient who developed severe exacerbation of type 2 diabetes mellitus after the initiation of olanzapine therapy. CASE SUMMARY: A 54-year-old African-American woman developed severe glucose dysregulation 12 days after the initiation of olanzapine. Prior to starting olanzapine therapy, the patient's diabetes was controlled by diet modification with a glycosylated hemoglobin of 6.5%. During olanzapine therapy, blood glucose concentrations could not be regulated despite use of antidiabetic agents, insulin, and dietary interventions. The patient also gained a total of 13 kg. Two weeks after discontinuation of all antipsychotic medications (olanzapine, quetiapine), the patient's blood glucose concentrations became better regulated and remained better controlled until discharge. DISCUSSION: All atypical antipsychotics are

associated with weight gain. **Obesity** is a well-documented risk factor for developing type 2 diabetes mellitus. Currently there are only six published reports that implicate olanzapine as being associated with glucose dysregulation. The exact cause of glucose dysregulation with olanzapine is unclear, but weight gain does not seem to be the sole etiology. It has been hypothesized that serotonin (5-**HT1A**) antagonism may decrease the responsiveness of the pancreatic beta-cells. This would then result in inappropriately low insulin secretion and, therefore, hyperglycemia. Based on the Naranjo probability scale, the likelihood that olanzapine caused the glucose dysregulation in our patient was possible. CONCLUSIONS: Although olanzapine has shown greater clinical efficacy and is associated with fewer extrapyramidal side effects than typical antipsychotics, it may produce exacerbation or new emergence of diabetes mellitus. Further examination of the incidence and etiology of glucose dysregulation after the initiation of olanzapine therapy is necessary.

L4 ANSWER 3 OF 8 MEDLINE on STN
AN 1998256091 MEDLINE
DN PubMed ID: 9593827
TI The 5-**HT1A** and 5-HT2A/2C receptor antagonists WAY-100635 and ritanserin do not attenuate D-fenfluramine-induced fos expression in the brain.
AU Javed A; Van de Kar L D; Gray T S
CS Neuroscience Program, Loyola University of Chicago School of Medicine, Maywood, IL 60153, USA.
NC NS 20041 (NINDS)
NS 34153 (NINDS)
SO Brain research, (1998 Apr 27) 791 (1-2) 67-74.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980803
AB D-Fenfluramine is a serotonin (5-hydroxytryptamine, 5-HT) releaser and reuptake inhibitor. It is used to study the neurochemical control of feeding and has been used to treat **obesity**. It has also been employed as a pharmacological tool to study changes in serotonergic function in psychiatric patients. Brain sites activated by D-fenfluramine via the release of 5-HT have been mapped via the expression of the immediate early gene c-fos. Studies in our laboratory have indicated that D-fenfluramine induces Fos in the hypothalamus and cortex through 5-HT release. The present study investigated whether 5-HT released by D-fenfluramine induces Fos expression in the brain by activating 5-**HT1A** or 5-HT2A/2C receptors. Rats were pretreated either with WAY-100635, a 5-**HT1A** antagonist, or ritanserin, a 5-HT2A/2C antagonist, prior to d-fenfluramine injection. Blockade of either 5-**HT1A** or 5-HT2A/2C receptors was not sufficient to suppress the Fos response to D-fenfluramine in any region of the brain examined, including the cingulate cortex, frontal cortex, caudate-putamen, paraventricular nucleus of the hypothalamus, amygdala, and brainstem. These results indicate that Fos response elicited by D-fenfluramine may be mediated by other receptors, in addition to the 5-**HT1A** or 5-HT2A/2C receptors.

L4 ANSWER 4 OF 8 MEDLINE on STN
AN 1998176038 MEDLINE
DN PubMed ID: 9507085
TI **5HT1A** receptor antagonists enhance the functional activity of fluoxetine in a mouse model of feeding.
AU Li D L; Simmons R M; Iyengar S
CS Lilly Neuroscience, Mail Code 0510, Lilly Research Laboratories, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285, USA.
SO Brain research, (1998 Jan 19) 781 (1-2) 119-26.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980507

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Last Updated on STN: 19980507
Entered Medline: 19980429

AB Fluoxetine has been reported to suppress food intake in animal models of feeding. Fluoxetine increases extracellular serotonin in the brain. **5HT1A** autoreceptors regulate synaptic levels of serotonin. A combination of a **5HT1A** receptor antagonist and fluoxetine has been previously reported to enhance extracellular levels of serotonin over what is obtained with fluoxetine alone. Thus, a combination of fluoxetine and a **5HT1A** antagonist could enhance the ability of fluoxetine to suppress appetite. Fluoxetine was tested in a model of feeding, in which CD-1 mice were trained to drink sweetened condensed milk. Fluoxetine was found to attenuate milk drinking, in a dose-dependent manner, at doses greater than 10 mg/kg, i.p. A 10 mg/kg dose of fluoxetine, which was ineffective by itself, was then combined either with 5-hydroxytryptophan (5HTP), a serotonin precursor, or with S(-) pindolol, a **5HT1A**/beta adrenergic receptor antagonist or with LY206130, a more selective **5HT1A** receptor antagonist. These treatment paradigms resulted in significant attenuation of the consumption of sweetened condensed milk. Since fluoxetine has been shown to be useful in the treatment of eating disorders and to promote weight loss in obese humans, although at doses greater than those required for the treatment of depression, a combination of fluoxetine with a **5HT1A** receptor antagonist could be of clinical utility in the treatment of eating disorders and **obesity**.

L4 ANSWER 5 OF 8 MEDLINE on STN
AN 96235878 MEDLINE
DN PubMed ID: 8697043
TI Multiple serotonin receptors: opportunities for new treatments for **obesity**?.
AU Dourish C T
CS Department of Neuropharmacology, Wyeth Research UK Ltd., Maidenhead, Berkshire, UK.
SO Obesity research, (1995 Nov) 3 Suppl 4 449S-462S. Ref: 108
Journal code: 9305691. ISSN: 1071-7323.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199609
ED Entered STN: 19960912
Last Updated on STN: 19970203
Entered Medline: 19960905

AB Recent progress in the molecular pharmacology of 5-HT receptors and the development of selective ligands for various 5-HT receptor subtypes has advanced our understanding of the role of 5-HT mechanisms in the control of food intake and bodyweight. The most intensively investigated 5-HT receptor subtypes have been the 5-**HT1A** receptor, the 5-HT1B receptor and the 5-HT2C receptor. The overall pattern of results to date suggests that selective 5-HT2C agonists may be novel anorectic drugs and prove useful in the treatment of **obesity**. However, a number of issues remain unresolved, particularly regarding potential side-effects, as the 5-HT2C receptor agonist mCPP has been reported to induce anxiety and nausea in humans, actions that would clearly limit its therapeutic utility. In addition, the possible role of recently cloned 5-HT receptor subtypes such as 5-ht5, 5-ht6 and 5-ht7, remains unexplored and the development of selective ligands for these sites has the potential to lead to new treatments for **obesity**.

L4 ANSWER 6 OF 8 MEDLINE on STN
AN 94298903 MEDLINE
DN PubMed ID: 8026551
TI 8-OH-DPAT induces a selective increase in protein intake in ageing overweight animals.
AU Lacour F; Berger S; Espinal J; Duhault J
CS Division of Metabolic Diseases, Institut de Recherches Servier, Suresnes, France.
SO European journal of pharmacology, (1994 Apr 1) 255 (1-3) 249-52.
Journal code: 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

106663533

EM 199408
ED Entered STN: 19940818
Last Updated on STN: 19940818
Entered Medline: 19940808
AB We have examined the effects of a 5-**HT1A** receptor agonist (8-hydroxy-2-(di-n-propylamino)tetralin, 8-OH-DPAT) on food preference in ageing rats that had been given a 'palatable' meal 15 min before administration of the drug. Ageing rats consumed a greater amount of the 'palatable' pre-meal than the young rats. In young rats lipids were the predominant source of calories, but in old animals lipid and protein consumption was similar. Administration of 8-OH-DPAT resulted in an increase in total caloric intake in both groups. Concomitant with this there was a significant increase in protein intake in both groups, which was most important in ageing rats, where proteins became the predominant source of calories.

L4 ANSWER 7 OF 8 MEDLINE on STN
AN 91359850 MEDLINE
DN PubMed ID: 1653393
TI Effects of repeated administration of mifepristone and 8-OH-DPAT on expression of preproneuropeptide Y mRNA in the arcuate nucleus of obese Zucker rats.
AU Pesonen U; Rouru J; Huupponen R; Koulu M
CS Department of Pharmacology, University of Turku, Finland.
SO Brain research. Molecular brain research, (1991 Jun) 10 (3) 267-72.
Journal code: 8908640. ISSN: 0169-328X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199110
ED Entered STN: 19911027
Last Updated on STN: 19970203
Entered Medline: 19911007
AB Neuropeptide Y (NPY) is an important hypothalamic regulator of feeding behavior. In this study we have investigated the regulation of the expression of preproNPY mRNA in male obese and lean Zucker rats by in situ hybridization. These animals represent a model of genetic **obesity** with hyperphagia, hyperinsulinemia and altered endocrine functions. Obese Zucker rats, treated for 12 days with 0.9% saline, had about 210% higher level of basal preproNPY mRNA expression in the arcuate nucleus when compared to their lean littermate controls. Repeated administrations of 8-hydroxy-dipropylaminotetralin (8-OH-DPAT), a serotonergic 5-**HT1A** agonist, or mifepristone, a glucocorticoid receptor antagonist, did not modify the basal expression of preproNPY mRNA in the Zucker phenotypes. The 8-OH-DPAT treatment significantly reduced hyperinsulinemia in obese Zucker rats without changing plasma glucose levels. The mifepristone treatment significantly increased plasma corticosterone levels in lean animals, but not in obese animals. The present study demonstrates enhanced expression of preproNPY mRNA in the arcuate nucleus in obese Zucker rats suggesting an involvement of NPY in the pathophysiology of the hyperphagic syndrome and genetically determined **obesity** in Zucker rats. Neither the antagonism of glucocorticoid receptors by mifepristone, nor repeated treatment with 8-OH-DPAT resulting in reduced insulin levels in obese Zucker rats, modified the basal expression of preproNPY mRNA in the arcuate nucleus.

L4 ANSWER 8 OF 8 MEDLINE on STN
AN 88225227 MEDLINE
DN PubMed ID: 2967189
TI Hyperinsulinemia of the genetically obese (fa/fa) rat is decreased by a low dose of the 5-**HT1A** receptor agonist 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT).
AU Chaouloff F; Jeanrenaud B
CS Laboratoire de Pharmacologie, INSERM U7, CHU Necker-Enfants Malades, Paris, France.
SO European journal of pharmacology, (1988 Feb 16) 147 (1) 111-8.
Journal code: 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198806
ED Entered STN: 19900308
Last Updated on STN: 19900308
Entered Medline: 19880628

106663533

AB Changes in glycemia and insulinemia were determined in conscious lean (FA/?) and obese (fa/fa) rats after acute administration of the 5-**HT1A** receptor agonist 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT). The intravenous injection of a low dose of 8-OH-DPAT (150 micrograms/kg) to lean rats rapidly promoted hyperglycemia. This modification was associated with a slight increase in insulinemia. The injection of 8-OH-DPAT markedly decreased basal hyperinsulinemia in obese rats while inducing hyperglycemia. Further evidence of the strong inhibitory effect of 8-OH-DPAT on insulin release was obtained in lean and obese rats during glucose tolerance tests. Intracerebroventricular injection of 8-OH-DPAT (45 micrograms/animal) triggered hyperglycemia and markedly decreased insulinemia in both lean and obese rats. This hypoinsulinemic effect of 8-OH-DPAT was more pronounced in the obese than in the lean animals. Measurement of the food intake elicited by 8-OH-DPAT (500 micrograms/kg s.c.) showed that the hyperphagic action of the 5-**HT1A** agonist was the same in FA/? and fa/fa rats. It is suggested that: (i) hyperinsulinemia of the genetically obese rat may be diminished by a low dose of 8-OH-DPAT; (ii) 5-**HT1A** autoreceptor-mediated regulation of serotonergic activity is not different in lean (FA/?) and obese (fa/fa) rats; (iii) 8-OH-DPAT could be of potential therapeutic use for some aspects of the pathology of type II diabetes.

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> d 1-4 bib abs kwic

L9 ANSWER 1 OF 4 MEDLINE on STN
AN 2001644973 MEDLINE
DN PubMed ID: 11697445
TI Investigations on possible serotonergic involvement in effects of OB-200G (polyherbal preparation) on food intake in female mice.
AU Kaur G; Kulkarni S K
CS Pharmacology Division, Univ Inst Pharm Sci, Panjab University, Chandigarh, India.
SO European journal of nutrition, (2001 Jun) 40 (3) 127-33.
Journal code: 100888704. ISSN: 1436-6207.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200112
ED Entered STN: 20011108
Last Updated on STN: 20020123
Entered Medline: 20011205
AB BACKGROUND: OB-200G is a polyherbal preparation containing aqueous extracts of Garcinia cambogia, Gymnema sylvestre, Zingiber officinale, Piper longum and resin from Commiphora mukul, all possessing thermogenic properties. Our previous studies reveal OB-200G to exert antiobesity effects in dietary animal models of **obesity**. AIM OF THE STUDY: The present study investigated the possible involvement of serotonergic system in the effect of OB-200G on food intake. We examined the effects of systemic pretreatment with 5-HT depletor, p-chlorophenylalanine (PCPA, 300 mg/kg, i. p. for 6 days), 5-**HT1A** agonist, (8-hydroxy-2-(di-N-propylamino)-tetralin (8-OH-DPAT, 0.1 mg/kg, i. p.), nonselective 5-HT **antagonist**, cyproheptadine (1 mg/kg, i. p.), 5-HT2 receptor **antagonist**, seganserin (1 and 2 mg/kg, i. p.) and 2-deoxy-D-glucose (2-DG, glucose antimetabolite, 500 mg/kg, i. p.) on satiety induced by OB-200G (500 mg/kg, p. o.) in non-deprived female mice. The results were compared with fluoxetine (10 mg/kg, i. p.), a selective serotonin reuptake inhibitor. METHODS: Fifteen minutes after the last drug administration, groups of mice were presented with sweetened chow and the amount of food consumed was recorded at 0.5,1,2, 3 and 4h time intervals. RESULTS: The hyperphagic effect of PCPA, 8-OH-DPAT, cyproheptadine and 2-DG was significantly ($p < 0.05$) antagonized by both OB-200G and fluoxetine. However, the anorectic effect of fluoxetine was not reversed by centrally acting 5-HT2 **antagonist**, seganserin but the latter markedly attenuated the satiety action of OB-200G. CONCLUSION: The present observations suggest the role of serotonin in mediation of satiety by OB-200G and hence its antiobesity effect.
AB . . . Commiphora mukul, all possessing thermogenic properties. Our previous studies reveal OB-200G to exert antiobesity effects in dietary animal models of **obesity**. AIM OF THE STUDY: The present study investigated the possible involvement of serotonergic system in the effect of OB-200G on. . . intake. We examined the effects of systemic pretreatment with 5-HT depletor, p-chlorophenylalanine (PCPA, 300 mg/kg, i. p. for 6 days), 5-**HT1A** agonist, (8-hydroxy-2-(di-N-propylamino)-tetralin (8-OH-DPAT, 0.1 mg/kg, i. p.), nonselective 5-HT **antagonist**, cyproheptadine (1 mg/kg, i. p.), 5-HT2 receptor **antagonist**, seganserin (1 and 2 mg/kg, i. p.) and 2-deoxy-D-glucose (2-DG, glucose antimetabolite, 500 mg/kg, i. p.) on satiety induced by. . . 0.05) antagonized by both OB-200G and fluoxetine. However, the anorectic effect of fluoxetine was not reversed by centrally acting 5-HT2 **antagonist**, seganserin but the latter markedly attenuated the satiety action of OB-200G. CONCLUSION: The present observations suggest the role of serotonin. . .

L9 ANSWER 2 OF 4 MEDLINE on STN
AN 1998256091 MEDLINE
DN PubMed ID: 9593827
TI The 5-**HT1A** and 5-HT2A/2C receptor **antagonists** WAY-100635 and ritanserin do not attenuate D-fenfluramine-induced fos expression in the brain.
AU Javed A; Van de Kar L D; Gray T S
CS Neuroscience Program, Loyola University of Chicago School of Medicine, Maywood, IL 60153, USA.
NC NS 20041 (NINDS)
NS 34153 (NINDS)
SO Brain research, (1998 Apr 27) 791 (1-2) 67-74.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands

106663533

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980803
AB D-Fenfluramine is a serotonin (5-hydroxytryptamine, 5-HT) releaser and reuptake inhibitor. It is used to study the neurochemical control of feeding and has been used to treat **obesity**. It has also been employed as a pharmacological tool to study changes in serotonergic function in psychiatric patients. Brain sites activated by D-fenfluramine via the release of 5-HT have been mapped via the expression of the immediate early gene c-fos. Studies in our laboratory have indicated that D-fenfluramine induces Fos in the hypothalamus and cortex through 5-HT release. The present study investigated whether 5-HT released by D-fenfluramine induces Fos expression in the brain by activating 5-**HT1A** or 5-HT2A/2C receptors. Rats were pretreated either with WAY-100635, a 5-**HT1A antagonist**, or ritanserin, a 5-HT2A/2C **antagonist**, prior to d-fenfluramine injection. Blockade of either 5-**HT1A** or 5-HT2A/2C receptors was not sufficient to suppress the Fos response to D-fenfluramine in any region of the brain examined, including the cingulate cortex, frontal cortex, caudate-putamen, paraventricular nucleus of the hypothalamus, amygdala, and brainstem. These results indicate that Fos response elicited by D-fenfluramine may be mediated by other receptors, in addition to the 5-**HT1A** or 5-HT2A/2C receptors.

TI The 5-**HT1A** and 5-HT2A/2C receptor **antagonists** WAY-100635 and ritanserin do not attenuate D-fenfluramine-induced fos expression in the brain.
AB . . . releaser and reuptake inhibitor. It is used to study the neurochemical control of feeding and has been used to treat **obesity**. It has also been employed as a pharmacological tool to study changes in serotonergic function in psychiatric patients. Brain sites. . . through 5-HT release. The present study investigated whether 5-HT released by D-fenfluramine induces Fos expression in the brain by activating 5-**HT1A** or 5-HT2A/2C receptors. Rats were pretreated either with WAY-100635, a 5-**HT1A antagonist**, or ritanserin, a 5-HT2A/2C **antagonist**, prior to d-fenfluramine injection. Blockade of either 5-**HT1A** or 5-HT2A/2C receptors was not sufficient to suppress the Fos response to D-fenfluramine in any region of the brain examined, . . . brainstem. These results indicate that Fos response elicited by D-fenfluramine may be mediated by other receptors, in addition to the 5-**HT1A** or 5-HT2A/2C receptors.

L9 ANSWER 3 OF 4 MEDLINE on STN
AN 1998176038 MEDLINE
DN PubMed ID: 9507085
TI **5HT1A** receptor **antagonists** enhance the functional activity of fluoxetine in a mouse model of feeding.
AU Li D L; Simmons R M; Iyengar S
CS Lilly Neuroscience, Mail Code 0510, Lilly Research Laboratories, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285, USA.
SO Brain research, (1998 Jan 19) 781 (1-2) 119-26.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980429
AB Fluoxetine has been reported to suppress food intake in animal models of feeding. Fluoxetine increases extracellular serotonin in the brain. **5HT1A** autoreceptors regulate synaptic levels of serotonin. A combination of a **5HT1A** receptor **antagonist** and fluoxetine has been previously reported to enhance extracellular levels of serotonin over what is obtained with fluoxetine alone. Thus, a combination of fluoxetine and a **5HT1A antagonist** could enhance the ability of fluoxetine to suppress appetite. Fluoxetine was tested in a model of feeding, in which CD-1 mice were trained to drink sweetened condensed milk. Fluoxetine was found to attenuate milk drinking, in a dose-dependent manner, at doses greater than 10 mg/kg, i.p.

A 10 mg/kg dose of fluoxetine, which was ineffective by itself, was then combined either with 5-hydroxytryptophan (5HTP), a serotonin precursor, or with S(-) pindolol, a **5HT1A**/beta adrenergic receptor **antagonist** or with LY206130, a more selective **5HT1A** receptor **antagonist**. These treatment paradigms resulted in significant attenuation of the consumption of sweetened condensed milk. Since fluoxetine has been shown to be useful in the treatment of eating disorders and to promote weight loss in obese humans, although at doses greater than those required for the treatment of depression, a combination of fluoxetine with a **5HT1A** receptor **antagonist** could be of clinical utility in the treatment of eating disorders and **obesity**.

TI **5HT1A** receptor **antagonists** enhance the functional activity of fluoxetine in a mouse model of feeding.

AB . . . Fluoxetine has been reported to suppress food intake in animal models of feeding. Fluoxetine increases extracellular serotonin in the brain. **5HT1A** autoreceptors regulate synaptic levels of serotonin. A combination of a **5HT1A** receptor **antagonist** and fluoxetine has been previously reported to enhance extracellular levels of serotonin over what is obtained with fluoxetine alone. Thus, a combination of fluoxetine and a **5HT1A antagonist** could enhance the ability of fluoxetine to suppress appetite. Fluoxetine was tested in a model of feeding, in which CD-1. . . which was ineffective by itself, was then combined either with 5-hydroxytryptophan (5HTP), a serotonin precursor, or with S(-) pindolol, a **5HT1A**/beta adrenergic receptor **antagonist** or with LY206130, a more selective **5HT1A** receptor **antagonist**. These treatment paradigms resulted in significant attenuation of the consumption of sweetened condensed milk. Since fluoxetine has been shown to. . . obese humans, although at doses greater than those required for the treatment of depression, a combination of fluoxetine with a **5HT1A** receptor **antagonist** could be of clinical utility in the treatment of eating disorders and **obesity**.

L9 ANSWER 4 OF 4 MEDLINE on STN
AN 91359850 MEDLINE
DN PubMed ID: 1653393
TI Effects of repeated administration of mifepristone and 8-OH-DPAT on expression of preproneuropeptide Y mRNA in the arcuate nucleus of obese Zucker rats.
AU Pesonen U; Rouru J; Huupponen R; Koulu M
CS Department of Pharmacology, University of Turku, Finland.
SO Brain research. Molecular brain research, (1991 Jun) 10 (3) 267-72.
Journal code: 8908640. ISSN: 0169-328X.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199110
ED Entered STN: 19911027
Last Updated on STN: 19970203
Entered Medline: 19911007

AB Neuropeptide Y (NPY) is an important hypothalamic regulator of feeding behavior. In this study we have investigated the regulation of the expression of preproNPY mRNA in male obese and lean Zucker rats by in situ hybridization. These animals represent a model of genetic **obesity** with hyperphagia, hyperinsulinemia and altered endocrine functions. Obese Zucker rats, treated for 12 days with 0.9% saline, had about 210% higher level of basal preproNPY mRNA expression in the arcuate nucleus when compared to their lean littermate controls. Repeated administrations of 8-hydroxy-dipropylaminotetralin (8-OH-DPAT), a serotonergic 5-**HT1A** agonist, or mifepristone, a glucocorticoid receptor **antagonist**, did not modify the basal expression of preproNPY mRNA in the Zucker phenotypes. The 8-OH-DPAT treatment significantly reduced hyperinsulinemia in obese Zucker rats without changing plasma glucose levels. The mifepristone treatment significantly increased plasma corticosterone levels in lean animals, but not in obese animals. The present study demonstrates enhanced expression of preproNPY mRNA in the arcuate nucleus in obese Zucker rats suggesting an involvement of NPY in the pathophysiology of the hyperphagic syndrome and genetically determined **obesity** in Zucker rats. Neither the antagonism of glucocorticoid receptors by mifepristone, nor repeated treatment with 8-OH-DPAT resulting in reduced insulin levels in obese Zucker rats, modified the basal expression of preproNPY mRNA in the arcuate nucleus.

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AB . . . preproNPY mRNA in male obese and lean Zucker rats by in situ hybridization. These animals represent a model of genetic **obesity** with hyperphagia, hyperinsulinemia and altered endocrine functions. Obese Zucker rats, treated for 12 days with 0.9% saline, had about 210%. . . mRNA expression in the arcuate nucleus when compared to their lean littermate controls. Repeated administrations of 8-hydroxy-dipropylaminotetralin (8-OH-DPAT), a serotonergic 5-**HT1A** agonist, or mifepristone, a glucocorticoid receptor **antagonist**, did not modify the basal expression of preproNPY mRNA in the Zucker phenotypes. The 8-OH-DPAT treatment significantly reduced hyperinsulinemia in. . . nucleus in obese Zucker rats suggesting an involvement of NPY in the pathophysiology of the hyperphagic syndrome and genetically determined **obesity** in Zucker rats. Neither the antagonism of glucocorticoid receptors by mifepristone, nor repeated treatment with 8-OH-DPAT resulting in reduced insulin. . .

CT . . .

BL, blood
Gene Expression: DE, drug effects
Insulin: BL, blood
*Mifepristone: PD, pharmacology
*Neuropeptide Y: GE, genetics
Nucleic Acid Hybridization
Obesity: PP, physiopathology
*Protein Precursors: GE, genetics
RNA, Messenger: AN, analysis
*RNA, Messenger: GE, genetics
Rats
Rats, Zucker
Reference Values

. . .

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=> d 1-3 bib abs

L13 ANSWER 1 OF 3 MEDLINE on STN
AN 2001154655 MEDLINE
DN PubMed ID: 11202445
TI Visualisation of serotonin-1A (5-HT1A) receptors in the central nervous system.
AU Passchier J; van Waarde A
CS PET Center, University Hospital Groningen, The Netherlands.
SO European journal of nuclear medicine, (2001 Jan) 28 (1) 113-29. Ref: 131
Journal code: 7606882. ISSN: 0340-6997.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20030118
Entered Medline: 20010322
AB The 5-**HT1A** subtype of receptors for the neurotransmitter serotonin is predominantly located in the limbic forebrain and is involved in the modulation of emotion and the function of the hypothalamus. Since 5-**HT1A** receptors are implicated in the pathogenesis of anxiety, depression, hallucinogenic behaviour, motion sickness and **eating disorders**, they are an important target for drug therapy. Here, we review the radioligands which are available for visualisation and quantification of this important neuroreceptor in the human brain, using positron emission tomography (PET) or single-photon emission tomography (SPET). More than 20 compounds have been labelled with carbon-11 (half-life 20 min), fluorine-18 (half-life 109.8 min) or iodine-123 (half-life 13.2 h): structural analogues of the agonist, 8-OH-DPAT, structural analogues of the **antagonist**, WAY 100635, and apomorphines. The most successful radioligands thus far are [carbonyl-11C] WAY-100635 (WAY), [carbonyl-11C]desmethyl-WAY-100635 (DWAY), p-[18F]MPPF and [11C]robalzotan (NAD-299). The high-affinity ligands WAY and DWAY produce excellent images of 5-**HT1A** receptor distribution in the brain (even the raphe nuclei are visualised), but they cannot be distributed to remote facilities and they probably cannot be used to measure changes in endogenous serotonin. Binding of the moderate-affinity ligands MPPF and NAD-299 may be more sensitive to serotonin competition and MPPF can be distributed to PET centres within a flying distance of a few hours. Future research should be directed towards: (a) improvement of the metabolic stability in primates; (b) development of a fluorinated radioligand which can be produced in large quantities and (c) production of a radioiodinated or technetium-labelled ligand for SPET.

L13 ANSWER 2 OF 3 MEDLINE on STN
AN 90122165 MEDLINE
DN PubMed ID: 2692641
TI Is there a relationship between serotonin receptor subtypes and selectivity of response in specific psychiatric illnesses?.
AU Montgomery S A; Fineberg N
CS St Mary's Hospital Medical School, London.
SO British journal of psychiatry. Supplement, (1989 Dec) (8) 63-9. Ref: 40
Journal code: 9001294. ISSN: 0960-5371.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199003
ED Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19900315
AB Identification of 5-HT receptor subtypes--5-**HT1A**, 5-HT1B, 5-HT1C, 5-HT1D, 5-HT2 (possibly A and B), 5-HT3 subtypes, and possibly 5-HT4--has encouraged the manufacture of 5-HT receptor inhibitors with greater subtype specificity. However, it appears that the receptors interact, and drugs initially thought to be specific may have multiple actions. For some conditions such as anxiety/depression, almost all receptors are implicated. Clinical studies provide clear evidence that manipulation of the 5-HT system has a role in treating depression,

anxiety, obsessional illness, migraine, and **eating disorders**. Interactions between the various receptor subtypes make it difficult to identify specific clinical functions. The 5-**HT1A** receptors may be involved in aggression, anorexia, and hypotension. The 5-HT1B receptors may be involved in aggression, while the 5-HT1C receptors may play a role in central aversion systems and anxiety/depression. The role of the 5-HT1D receptors remains speculative; 5-HT2 receptors appear to be involved in depression, anxiety, appetite, sleep, vasoconstriction, and hypertension. Many drugs that are effective in treating migraine are potent 5-HT2 **antagonists**. 5-HT3 **antagonists** at high doses are effective in treating nausea and at low doses in treating anxiety. Treatment of aggression, suicidal behaviour, addiction behaviour, memory impairment, dementia, and schizophrenia with 5-HT inhibitors requires further testing.

L13 ANSWER 3 OF 3 MEDLINE on STN
AN 88329202 MEDLINE
DN PubMed ID: 2970974
TI Evidence that the hyperphagic response to 8-OH-DPAT is mediated by 5-HT1A receptors.
AU Hutson P H; Dourish C T; Curzon G
CS Department of Neurochemistry, Institute of Neurology, Queen Square, London, U.K.
SO European journal of pharmacology, (1988 Jun 10) 150 (3) 361-6.
Journal code: 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198810
ED Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19881018
AB The 5-**HT1A** agonist, 8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT) at a dose of 1 mg/kg s.c. increased food intake in free feeding rats. 8-OH-DPAT-induced feeding was blocked by metergoline which has comparable affinity for 5-**HT1A**, 5-HT1B, 5-HT1C and 5-HT2 receptors. This is consistent with the hyperphagia being mediated by an action at 5-HT receptors. Evidence against the involvement of 5-HT2 or 5-HT3 receptors was provided by the lack of effect of methysergide, ketanserin, MDL 72222 and ICS 205930 on the feeding response. Blockade of the hyperphagia by (-)- but not (+)pendolol which stereoselectively interacts with 5-HT1 receptors indicated an involvement of this receptor type. The lack of effect of ketanserin suggests that the 5-HT1C site is not involved as it has high affinity for both 5-HT2 and 5-HT1C receptors. Blockade of the hyperphagia by spiperone suggests mediation by 5-**HT1A** rather than 5-HT1B receptors. Although spiperone also blocks dopamine and alpha 2-adrenoreceptors, involvement of these sites is unlikely as neither the DA **antagonist** haloperidol nor the alpha 2-adrenoceptor **antagonist** idazoxan blocked 8-OH-DPAT-induced feeding. These results indicate that 8-OH-DPAT-induced feeding is mediated by 5-**HT1A** receptors.

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L17 ANSWER 1 OF 2 MEDLINE on STN
AN 1998256091 MEDLINE
DN PubMed ID: 9593827
TI The 5-HT1A and 5-HT2A/2C receptor antagonists WAY-100635 and ritanserin do not attenuate D-fenfluramine-induced fos expression in the brain.
AU Javed A; Van de Kar L D; Gray T S
CS Neuroscience Program, Loyola University of Chicago School of Medicine, Maywood, IL 60153, USA.
NC NS 20041 (NINDS)
NS 34153 (NINDS)
SO Brain research, (1998 Apr 27) 791 (1-2) 67-74.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980803
AB D-Fenfluramine is a serotonin (5-hydroxytryptamine, 5-HT) releaser and reuptake inhibitor. It is used to study the neurochemical control of feeding and has been used to treat **obesity**. It has also been employed as a pharmacological tool to study changes in serotonergic function in psychiatric patients. Brain sites activated by D-fenfluramine via the release of 5-HT have been mapped via the expression of the immediate early gene c-fos. Studies in our laboratory have indicated that D-fenfluramine induces Fos in the hypothalamus and cortex through 5-HT release. The present study investigated whether 5-HT released by D-fenfluramine induces Fos expression in the brain by activating 5-HT1A or 5-HT2A/2C receptors. Rats were pretreated either with WAY-100635, a 5-**HT1A antagonist**, or ritanserin, a 5-HT2A/2C antagonist, prior to d-fenfluramine injection. Blockade of either 5-HT1A or 5-HT2A/2C receptors was not sufficient to suppress the Fos response to D-fenfluramine in any region of the brain examined, including the cingulate cortex, frontal cortex, caudate-putamen, paraventricular nucleus of the hypothalamus, amygdala, and brainstem. These results indicate that Fos response elicited by D-fenfluramine may be mediated by other receptors, in addition to the 5-HT1A or 5-HT2A/2C receptors.

L17 ANSWER 2 OF 2 MEDLINE on STN
AN 1998176038 MEDLINE
DN PubMed ID: 9507085
TI 5HT1A receptor antagonists enhance the functional activity of fluoxetine in a mouse model of feeding.
AU Li D L; Simmons R M; Iyengar S
CS Lilly Neuroscience, Mail Code 0510, Lilly Research Laboratories, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285, USA.
SO Brain research, (1998 Jan 19) 781 (1-2) 119-26.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980429
AB Fluoxetine has been reported to suppress food intake in animal models of feeding. Fluoxetine increases extracellular serotonin in the brain. 5HT1A autoreceptors regulate synaptic levels of serotonin. A combination of a 5HT1A receptor antagonist and fluoxetine has been previously reported to enhance extracellular levels of serotonin over what is obtained with fluoxetine alone. Thus, a combination of fluoxetine and a **5HT1A antagonist** could enhance the ability of fluoxetine to suppress appetite. Fluoxetine was tested in a model of feeding, in which CD-1 mice were trained to drink sweetened condensed milk. Fluoxetine was found to attenuate milk drinking, in a dose-dependent manner, at doses greater than 10 mg/kg, i.p. A 10 mg/kg dose of fluoxetine, which was ineffective by itself, was then combined either with 5-hydroxytryptophan (5HTP), a serotonin precursor, or with S(-) pindolol, a 5HT1A/beta adrenergic receptor antagonist or with LY206130, a more selective 5HT1A receptor antagonist. These treatment paradigms resulted in significant attenuation

of the consumption of sweetened condensed milk. Since fluoxetine has been shown to be useful in the treatment of eating disorders and to promote weight loss in obese humans, although at doses greater than those required for the treatment of depression, a combination of fluoxetine with a 5HT1A receptor antagonist could be of clinical utility in the treatment of eating disorders and **obesity**.

=> s l16 and eating
45491 EATING
L18 3 L16 AND EATING

=> d 1-3 bib abs

L18 ANSWER 1 OF 3 MEDLINE on STN
AN 1998176038 MEDLINE
DN PubMed ID: 9507085
TI 5HT1A receptor antagonists enhance the functional activity of fluoxetine in a mouse model of feeding.
AU Li D L; Simmons R M; Iyengar S
CS Lilly Neuroscience, Mail Code 0510, Lilly Research Laboratories, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285, USA.
SO Brain research, (1998 Jan 19) 781 (1-2) 119-26.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199804
ED Entered STN: 19980507
Last Updated on STN: 19980507
Entered Medline: 19980429
AB Fluoxetine has been reported to suppress food intake in animal models of feeding. Fluoxetine increases extracellular serotonin in the brain. 5HT1A autoreceptors regulate synaptic levels of serotonin. A combination of a 5HT1A receptor antagonist and fluoxetine has been previously reported to enhance extracellular levels of serotonin over what is obtained with fluoxetine alone. Thus, a combination of fluoxetine and a **5HT1A antagonist** could enhance the ability of fluoxetine to suppress appetite. Fluoxetine was tested in a model of feeding, in which CD-1 mice were trained to drink sweetened condensed milk. Fluoxetine was found to attenuate milk drinking, in a dose-dependent manner, at doses greater than 10 mg/kg, i.p. A 10 mg/kg dose of fluoxetine, which was ineffective by itself, was then combined either with 5-hydroxytryptophan (5HTP), a serotonin precursor, or with S(-) pindolol, a 5HT1A/beta adrenergic receptor antagonist or with LY206130, a more selective 5HT1A receptor antagonist. These treatment paradigms resulted in significant attenuation of the consumption of sweetened condensed milk. Since fluoxetine has been shown to be useful in the treatment of **eating** disorders and to promote weight loss in obese humans, although at doses greater than those required for the treatment of depression, a combination of fluoxetine with a 5HT1A receptor antagonist could be of clinical utility in the treatment of **eating** disorders and obesity.

L18 ANSWER 2 OF 3 MEDLINE on STN
AN 95175787 MEDLINE
DN PubMed ID: 7870997
TI Ipsapirone and 8-OH-DPAT reduce ethanol preference in rats: involvement of presynaptic 5-HT1A receptors.
AU Schreiber R; Opitz K; Glaser T; De Vry J
CS Institute for Neurobiology, Department of Psychopharmacology, Cologne, Germany.
SO Psychopharmacology, (1993) 112 (1) 100-10.
Journal code: 7608025. ISSN: 0033-3158.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199503
ED Entered STN: 19950407
Last Updated on STN: 19950407
Entered Medline: 19950329
AB The selective serotonin(5-HT)1A receptor agonists 8-OH-DPAT and ipsapirone were tested in selectively inbred Wistar rats, with high preference

[70-90%: defined as the ratio of ethanol (EtOH) to total fluid intake] for EtOH (10% v/v) over water in a two-bottle free choice situation. Rats were injected shortly before the overnight test session (8:00 P.M.-8:00 A.M.). EtOH and water consumption were determined in 20-min intervals; food consumption after the session. 8-OH-DPAT (ED50: 2.4 mg/kg, SC) and ipsapirone (ED50: 12.5 mg/kg, SC) reduced EtOH preference in a dose-dependent manner. In addition, 8-OH-DPAT increased total fluid intake, whereas ipsapirone enhanced total food intake. The EtOH preference reduction was time-dependent and reached a maximum within the second 4 h after application of 8-OH-DPAT (-73%) and ipsapirone (-72%). The preference reducing effect of ipsapirone (20 mg/kg, PO) was completely blocked by the nonselective 5-**HT1A antagonist** spiperone (0.05 mg/kg, SC). Local application of 8-OH-DPAT (10 micrograms, 0.5 microliters) into the dorsal raphe nucleus (DRN, a brain area rich in somatodendritic 5-HT1A autoreceptors), reduced the EtOH preference significantly as compared to the saline injection in the same animal (-12%, 8:00-12:00 P.M.). Only marginal effects on ingestion behavior were observed after microinjection into the nucleus accumbens. Reduction of brain 5-HT levels by pretreatment with the 5-HT synthesis inhibitor pCPA (2 x 150 mg/kg, IP) resulted in a short lasting, marked reduction (-54%) and a long lasting, small attenuation of the EtOH preference. Total food consumption was strongly decreased but returned soon to normal; total fluid intake was only slightly decreased. The EtOH preference reducing effect of ipsapirone (5 and 20 mg/kg, SC) was attenuated in pCPA-pretreated rats. The present data suggest that 5-HT1A receptor ligands reduce EtOH preference via stimulation of 5-HT1A receptors in the DRN. The possibility of additional mechanism(s) is discussed.

L18 ANSWER 3 OF 3 MEDLINE on STN
AN 90160980 MEDLINE
DN PubMed ID: 2137632
TI A pharmacological analysis of the **eating** response induced by 8-OH-DPAT injected into the dorsal raphe nucleus reveals the involvement of a dopaminergic mechanism.
AU Fletcher P J; Davies M
CS Neuropsychiatric Research Unit, University of Saskatchewan, Saskatoon, Canada.
SO Psychopharmacology, (1990) 100 (2) 188-94.
Journal code: 7608025. ISSN: 0033-3158.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199003
ED Entered STN: 19900601
Last Updated on STN: 19900601
Entered Medline: 19900327
AB Direct injection of the 5-hydroxytryptamine (5-HT) agonist 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) into the dorsal raphe nucleus (DRN) dose dependently increased food intake in free feeding rats. The hypothesis that this effect is mediated by 5-HT1A receptors was tested by investigating the abilities of the putative 5-**HT1A antagonists** metergoline, propranolol and spiperone to prevent 8-OH-DPAT-induced **eating**. Metergoline failed to affect 8-OH-DPAT-induced **eating** when injected either peripherally or into the DRN. Peripherally injected propranolol and spiperone prevented 8-OH-DPAT-induced **eating**, but these drugs were ineffective when injected into the DRN. These results indicate that 8-OH-DPAT-induced **eating** may not involve 5-HT1A receptors within the DRN. The ability of peripherally injected spiperone to prevent the **eating** response to 8-OH-DPAT reflects its dopamine blocking activity since haloperidol was an effective antagonist of 8-OH-DPAT-**eating**. This result may indicate that 8-OH-DPAT produces a general behavioural activation by reducing the inhibitory influence which 5-HT normally exerts over the nigrostriatal dopamine pathway, and that this behavioural activation is expressed as **eating** when food is the most salient goal object present.

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L20 ANSWER 1 OF 1 MEDLINE on STN
AN 2002150429 MEDLINE
DN PubMed ID: 11882917
TI Supersensitivity of 5-HT1A autoreceptors and alpha2-adrenoceptors regulating monoamine synthesis in the brain of morphine-dependent rats.
AU Sastre-Coll Antoni; Esteban Susana; Garcia-Sevilla Jesus A
CS Laboratory of Neuropharmacology, Associate Unit of the Institute Cajal/CSIC, Department of Biology, University of the Balearic Islands, Cra. Valldemossa Km 7.5, 07071 Palma de Mallorca, Spain.
SO Naunyn-Schmiedeberg's archives of pharmacology, (2002 Mar) 365 (3) 210-9. Journal code: 0326264. ISSN: 0028-1298.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020308
Last Updated on STN: 20030118
Entered Medline: 20020722
AB The sensitivity of 5-HT1A serotonin receptors and alpha2-adrenoceptors (autoreceptors and heteroreceptors) modulating brain monoamine synthesis was investigated in rats during morphine treatment and after naloxone-precipitated withdrawal. The accumulation of 5-hydroxytryptophan (5-HTP) and 3,4-dihydroxyphenylalanine (DOPA) after decarboxylase inhibition was used as a measure of the rate of tryptophan and tyrosine hydroxylation in vivo. Acute morphine (3-100 mg/kg, 1 h) increased the synthesis of 5-HTP/5-HT in various brain regions (15%-35%) and that of DOPA/dopamine (DA) in striatum (28%-63%), but decreased the synthesis of DOPA/noradrenaline (NA) in hippocampus and cortex (20%-33%). Naloxone (2-60 mg/kg, 1 h) did not alter the synthesis of 5-HTP or DOPA in brain. Tolerance to the inhibitory effect of morphine on DOPA/NA synthesis and a sensitization to its stimulatory effects on DOPA/DA and 5-HTP/5-HT synthesis were observed after chronic morphine and/or in morphine-withdrawn rats. In morphine-dependent rats (tolerant and withdrawn states) the inhibitory effects of the 5-HT1A agonists 8-OH-DPAT and buspirone (0.1 mg/kg, 1 h), and that of the alpha2-adrenoceptor agonist clonidine (0.1 mg/kg, 1 h), on the synthesis of 5-HTP/5-HT were potentiated (25%-50%). Moreover, the effect of 8-OH-DPAT was antagonized by WAY 100135, a selective 5-**HT1A antagonist**. In morphine-dependent rats (tolerant state), the inhibitory effects of clonidine on the synthesis of DOPA/NA (hippocampus, hypothalamus) and DOPA/DA (striatum) also were potentiated (35%-55%). In summary, we conclude that morphine **addiction** is associated with supersensitivity of 5-HT1A serotonin receptors and alpha2-adrenoceptors (autoreceptors and heteroreceptors) that modulate the synthesis of monoamines in brain.

=> s l16 and sexual
82960 SEXUAL
L21 6 L16 AND SEXUAL

=> d 1-6 bib abs

L21 ANSWER 1 OF 6 MEDLINE on STN
AN 2001243225 MEDLINE
DN PubMed ID: 11164513
TI Exhaustion of the coital reflex in spinal male rats is reversed by the serotonergic agonist 8-OH-DPAT.
AU Carro-Juarez M; Rodriguez-Manzo G
CS Unidad de Posgrado, Escuela de Medicina Veterinaria y Zootecnia, Universidad Autonoma de Tlaxcala, C.P.90000, AP.37 Tlaxcala, Mexico.
SO Behavioural brain research, (2001 Jan 29) 118 (2) 161-8. Journal code: 8004872. ISSN: 0166-4328.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200105
ED Entered STN: 20010517
Last Updated on STN: 20030118
Entered Medline: 20010510
AB Previous studies from our laboratory have shown that the genital motor pattern associated to the coital reflex in spinal male rats becomes

exhausted when repeatedly evoked. Exhaustion of the genital motor pattern could be related to the **sexual** exhaustion phenomenon observed in copulating male rats. The present study was aimed to describe the features of coital reflex exhaustion and to determine if the 5-HT1A agonist 8-OH-DPAT was able to reverse exhaustion of this ejaculatory-like response. Additionally, the effect of pre-treatment with the 5-**HT1A antagonist** WAY 100635 on the 8-OH-DPAT induced motor response was evaluated. Results revealed that development of coital reflex exhaustion initiated with a progressive increase in the latency of response and was characterised by a change in the properties of the motor pattern itself. Once exhausted, i.v. administration of 8-OH-DPAT provoked the immediate expression of a potent motor pattern similar to the coital reflex, but in the absence of urethral stimulation. Injection of WAY 100635 induced, per se, expression of the coital reflex after exhaustion. Notwithstanding, pre-treatment with WAY 100635 was able to block the 8-OH-DPAT-induced motor response implying that its effect was exerted upon 5-HT1A receptors. Data suggest that the **sexual** exhaustion phenomenon might possess a spinal component.

L21 ANSWER 2 OF 6 MEDLINE on STN
AN 1999147862 MEDLINE
DN PubMed ID: 10023030
TI Partial antagonism of 8-OH-DPAT'S effects on male rat **sexual** behavior with a D2, but not a 5-**HT1A, antagonist.**
AU Matuszewich L; Lorrain D S; Trujillo R; Dominguez J; Putnam S K; Hull E M
CS Department of Psychology, Park Hall, State University of New York at Buffalo, Buffalo, NY 14260-4110, USA.
NC MH 40826 (NIMH)
SO Brain research, (1999 Feb 27) 820 (1-2) 55-62.
Journal code: 0045503. ISSN: 0006-8993.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199903
ED Entered STN: 19990413
Last Updated on STN: 20000303
Entered Medline: 19990329
AB The serotonin agonist 8-hydroxy-di-propylaminotetralin (8-OH-DPAT), injected systemically or directly into the medial preoptic area (MPOA), reduces the ejaculatory threshold in male rats. While 8-OH-DPAT has been characterized as an agonist at the 5-HT1A receptor, it also acts at other receptor sites including the dopamine D2 receptor. The current experiments investigated whether 8-OH-DPAT injected into the MPOA facilitates male **sexual** behavior through stimulation of the 5-HT1A receptor or the dopamine D2 receptor. Experiment 1 co-administered 8-OH-DPAT (6 microgram) with either the 5-**HT1A antagonist** 4-iodo-N-[2-[4-(methoxyphenyl)-1-piperazinyl]ethyl]-N-2-pyridinyl-ben zamide hydrochloride (MPPI) (10 microgram) or the D2 antagonist raclopride (10 microgram). Raclopride blocked 8-OH-DPAT's facilitative effects on ejaculation frequency and latency, while the 5-**HT1A antagonist** was ineffective. In Experiment 2, 8-OH-DPAT (500 microM), retrodialyzed into the MPOA through a microdialysis probe, enhanced male copulatory behavior similarly to the microinjection, increasing ejaculation frequency and decreasing ejaculation latency, postejaculatory interval and mount frequency. Retrodialyzing 8-OH-DPAT through a microdialysis probe in the MPOA had been previously shown to increase extracellular levels of dopamine and serotonin. The data from the present studies suggest that the effects of 8-OH-DPAT in the MPOA on male rat copulatory behavior may be mediated, at least in part, either directly through 8-OH-DPAT's activity at D2 receptors or indirectly through 8-OH-DPAT's ability to increase extracellular dopamine.

L21 ANSWER 3 OF 6 MEDLINE on STN
AN 1998256064 MEDLINE
DN PubMed ID: 9593901
TI 8-OH-DPAT influences extracellular levels of serotonin and dopamine in the medial preoptic area of male rats.
AU Lorrain D S; Matuszewich L; Hull E M
CS Department of Psychology, State University of New York at Buffalo, Buffalo, NY 14260-4110, USA.
NC MH 40826 (NIMH)
SO Brain research, (1998 Apr 20) 790 (1-2) 217-23.
Journal code: 0045503. ISSN: 0006-8993.

106663533

CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199807
ED Entered STN: 19980716
Last Updated on STN: 20030118
Entered Medline: 19980707
AB Serotonin (5-HT) is generally inhibitory to male rat **sexual** behavior. However, the 5-HT1A agonist 8-hydroxy-di-propylaminotetralin (8-OH-DPAT), injected either systemically or into the medial preoptic area (MPOA), facilitates ejaculation. Three experiments were conducted to test the effects of 8-OH-DPAT on 5-HT and dopamine (DA) neurotransmission in the MPOA, a very important site for the control of male **sexual** behavior. In Experiment 1, systemically injected 8-OH-DPAT (0.4 mg/kg) decreased extracellular 5-HT levels in the MPOA as measured by in vivo microdialysis. In Experiment 2, 8-OH-DPAT (500 microM) administered directly into the MPOA via reverse dialysis increased extracellular levels of both DA and 5-HT; pretreatment with the selective 5-**HT1A antagonist** 4-iodo-N-[2-[4-(methoxyphenyl)-1-piperazinyl]ethyl]-N-2-pyridinyl-ben benzamide hydrochloride (p-MPPI) failed to prevent 8-OH-DPAT's stimulatory effects on DA and 5-HT levels in the MPOA. In Experiment 3, 8-OH-DPAT (8 microg) co-injected with 5,7-dihydroxytryptamine (5,7-DHT; 6 microg) prevented neurotoxic depletion of 5-HT in the site of injection (MPOA). Because systemic and MPOA injections of 8-OH-DPAT resulted in opposite effects on extracellular 5-HT in the MPOA, yet both can facilitate ejaculation, these data suggest that moderate changes in 5-HT in the MPOA may have relatively little influence on male copulatory behavior. Instead, the facilitative effects of 8-OH-DPAT in the MPOA on male copulatory behavior may result, at least in part, from stimulatory effects of 8-OH-DPAT on DA transmission. Facilitative effects of systemic injections of 8-OH-DPAT may result from decreased 5-HT release in several sites.

L21 ANSWER 4 OF 6 MEDLINE on STN
AN 96292583 MEDLINE
DN PubMed ID: 8728558
TI Neonatal organizational effects of the 5-HT2 and 5-HT1A subsystems on adult behavior in the rat.
AU Gonzalez M I; Albonetti E; Siddiqui A; Farabollini F; Wilson C A
CS Department of Obstetrics and Gynaecology, St. George's Hospital Medical School, London, UK.
SO Pharmacology, biochemistry, and behavior, (1996 May) 54 (1) 195-203.
Journal code: 0367050. ISSN: 0091-3057.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961106
Last Updated on STN: 19961106
Entered Medline: 19961023
AB Males, females, neonatally androgenized females, and neonatally castrated males were treated over the second week of life with 0.25 mg/kg of either the 5-HT2 agonist 1-(2,5-dimethoxy-3-iodophenyl)-2-aminopropane HCl (DOI), the 5-HT2 antagonist ritanserin (Rit), the 5-HT1A agonist 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT), or the 5-**HT1A antagonist** WAY100135 (WAY). Exploration, anxiety, sociosexual preferences, and **sexual** behavior were measured in adulthood. Agents acting on 5-HT1A receptors do not appear to affect organization of any of the behavioral systems studied. DOI increased exploratory activity but in females only, which suggests that testosterone antagonizes the stimulatory effect of 5-HT2 activity on exploration. Neonatal ritanserin selectively reduced anxiety in females, and DOI had a similar effect in androgenized females. This indicates that neonatal 5-HT2 activity is anxiogenic in normal females, anxiolytic in androgenized females, and has no effect on anxiety in males. Males and androgenized females both showed a preference for the female teaser that was abolished by the 5-HT2 agonist, DOI. These results point out that 5-HT2 activity selectively suppresses heterosexual preference induced in the presence of neonatal testosterone. DOI also reduced both male **sexual** behavior in males and female **sexual** behavior in androgenized females. Thus, the 5-HT2 system antagonizes the action of testosterone in stimulating heterosexual orientation and **sexual** activity, and this is independent of genetic sex.

106663533

L21 ANSWER 5 OF 6 MEDLINE on STN
AN 92289905 MEDLINE
DN PubMed ID: 1601066
TI The selective 5-HT2 receptor antagonist amperozide attenuates 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane-induced inhibition of male rat **sexual** behavior.
AU Klint T; Dahlgren I L; Larsson K
CS Kabi-Pharmacia Therapeutics AB, Malmo, Sweden.
SO European journal of pharmacology, (1992 Mar 3) 212 (2-3) 241-6.
Journal code: 1254354. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199207
ED Entered STN: 19920724
Last Updated on STN: 19920724
Entered Medline: 19920713
AB This study was aimed at exploring the role of 5-HT2/5-HT1C neurotransmission in male rat **sexual** behavior. The administration of the 5-HT2/5-HT1C agonist, 1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI) (1 mg/kg), suppressed **sexual** activity in most of the animals. The suppressive effect of DOI was antagonized by treatment with amperozide, a selective 5-HT2 receptor antagonist, in doses which did not by themselves affect **sexual** activity. In addition, several other serotonin antagonists were tested with varying affinity profiles for 5-HT2/5-HT1C receptors, including ketanserin, ritanserin, and mesulergine. All these compounds antagonized the suppressive action of DOI. In contrast, no antagonizing effect was obtained by treatment with (-)-alprenolol, a 5-**HT1A antagonist**. The present findings suggest that 5-HT2/5-HT1C receptors might be involved in the neural control of male rat **sexual** behavior, presumably by exerting an inhibitory influence on the behavior.

L21 ANSWER 6 OF 6 MEDLINE on STN
AN 91017932 MEDLINE
DN PubMed ID: 1977175
TI Effects of four beta-adrenergic receptor antagonists on male rat **sexual** behavior.
AU Smith E R; Maurice J; Richardson R; Walter T; Davidson J M
CS Department of Molecular and Cellular Physiology, Stanford University School of Medicine, CA 94305-5426.
NC AG 01437 (NIA)
SO Pharmacology, biochemistry, and behavior, (1990 Aug) 36 (4) 713-7.
Journal code: 0367050. ISSN: 0091-3057.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199011
ED Entered STN: 19910117
Last Updated on STN: 19950206
Entered Medline: 19901114
AB Antihypertensive medication has been reported to cause serious **sexual** side effects in men. Frequently mentioned as causing **sexual** dysfunction are beta-adrenergic receptor antagonists. The purpose of this study was to examine in detail the effects of beta blockers on adult male rat **sexual** behavior. Thirty minutes following a single subcutaneous injection of propranolol, pindolol, atenolol or labetalol, mating tests were conducted. The mixed beta 1- and beta 2-adrenergic antagonists, propranolol and pindolol, profoundly inhibited male **sexual** behavior. At the 5 and 10 mg/kg doses, propranolol inhibited ejaculatory behavior to the extent that only 9.1 and 8.3% respectively showed the behavior while pindolol reduced this behavior to 36.4% (16 mg/kg). These drugs also adversely affected various parameters of behavior in a dose-dependent manner. The selective beta 1 antagonist, atenolol, had only minor effects and labetalol even less so at the doses tested. It was suggested that the strongly inhibitory effects of propranolol and pindolol on male rat sex behavior may well be due to their 5-**HT1A antagonistic** binding properties rather than their beta-antagonistic properties.

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=> d 1-3 bib abs

L22 ANSWER 1 OF 3 MEDLINE on STN
AN 2003461173 IN-PROCESS
DN PubMed ID: 12909675
TI 5-Hydroxytryptamine 1A receptors inhibit cold-induced sympathetically mediated cutaneous vasoconstriction in rabbits.
AU Ootsuka Y; Blessing W W
CS Departments of Physiology and Medicine, Centre for Neuroscience, Flinders University Medical Centre, Bedford Park, Adelaide, South Australia 5042, Australia.
SO Journal of physiology, (2003 Oct 1) 552 (Pt 1) 303-14.
Journal code: 0266262. ISSN: 0022-3751.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20031003
Last Updated on STN: 20031218
AB 5-**HT1A** receptor agonists lower body temperature. We have investigated whether activation of 5-**HT1A** receptors inhibits cutaneous sympathetic discharge so that dilatation of the cutaneous vascular bed lowers body temperature by increasing heat transfer to the environment. We measured ear pinna blood flow in conscious rabbits (with chronically implanted Doppler ultrasound flow probes), and postganglionic sympathetic **vasomotor** nerve activity in anaesthetized rabbits. Recordings from conscious rabbits were made in a cage at 26 degrees C and the rabbit was then transferred to a cage at 10 degrees C. The ear pinna Doppler signal fell from 56 +/- 4 cm s-1 in the 26 degrees C cage to 4 +/- 1 cm s-1 ($P < 0.0001$, $n = 24$) after 30 min in the 10 degrees C cage, and body temperature increased from 38.8 +/- 0.2 to 39.0 +/- 0.2 degrees C ($P < 0.01$, $n = 24$). The 5-**HT1A** agonist 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT; 0.1 mg kg-1 I.V.) reversed the cold-induced fall in ear pinna blood flow (Doppler signal increased from 5 +/- 1 to 55 +/- 8 cm s-1, $P < 0.001$, $n = 7$) within 5 min when administered 30 min after transfer to the 10 degrees C cage, and prevented the fall in ear pinna blood flow when administered before the rabbit was transferred to the 10 degrees C cage. Body temperature decreased after administration of 8-OH-DPAT. These changes were abolished by the specific 5-**HT1A** antagonist WAY-100635 (0.1 mg kg-1 I.V.). In anaesthetized rabbits, 8-OH-DPAT (0.1 mg kg-1 I.V.) reduced resting postganglionic cutaneous sympathetic **vasomotor** discharge, and prevented the increase normally elicited by cooling the trunk. Our experiments constitute the first demonstration that activation of 5-**HT1A** receptors powerfully inhibits cold-induced increases in cutaneous sympathetic **vasomotor** discharge, thereby dilating the cutaneous vascular bed and increasing transfer of heat to the environment.

L22 ANSWER 2 OF 3 MEDLINE on STN
AN 97460999 MEDLINE
DN PubMed ID: 9315366
TI Pretreatment with the dopamine agonist quinpirole inhibits central antihypertensive mechanisms in rats.
AU van den Buuse M; Tritton S B
CS Baker Medical Research Institute, Prahran, Victoria, Australia..
maarten.vandenbuuse@baker.edu.au
SO Clinical and experimental pharmacology & physiology, (1997 Sep-Oct) 24 (9-10) 661-6.
Journal code: 0425076. ISSN: 0305-1870.
CY Australia
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199711
ED Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971119
AB 1. Intravenous or central treatment of spontaneously hypertensive rats (SHR) with the dopamine D2 receptor agonist quinpirole caused a short-lasting pressor response with little effect on heart rate. 2. At 30 min after intravenous administration of quinpirole, the antihypertensive effect of rilmenidine was significantly inhibited. This interaction of quinpirole and rilmenidine was similarly observed when quinpirole was administered either intravenously (0.3 or 0.1 mg/kg), in the lateral cerebral ventricles (0.1 mg/kg) or intracisternally (0.1 mg/kg) or when rilmenidine was administered intravenously (1 mg/kg) or intracisternally

(0.1 mg/kg). 3. The apparent desensitization to the antihypertensive effect of rilmenidine 30 min after pretreatment with quinpirole was not observed after a 4 or 24 h interval. 4. These data suggest that quinpirole has prolonged effects on central sympathetic **vasomotor** mechanisms that are the target of centrally acting antihypertensive drugs. These and previous results show a functional interaction between central dopamine D2 receptor activation and sympathetic responses mediated by a wide range of different receptors, including imidazoline and 5-hydroxytryptamine 5-**HT1A**-receptors and alpha 2-adrenoceptors.

L22 ANSWER 3 OF 3 MEDLINE on STN
AN 88064262 MEDLINE
DN PubMed ID: 2446059
TI Serotonin agonists and antagonists in experimental hypertension.
AU Saxena P R; Bolt G R; Dhasmana K M
CS Department of Pharmacology, Erasmus University Rotterdam, The Netherlands.
SO Journal of cardiovascular pharmacology, (1987) 10 Suppl 3 S12-8. Ref: 39
Journal code: 7902492. ISSN: 0160-2446.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 198801
ED Entered STN: 19900305
Last Updated on STN: 19900305
Entered Medline: 19880107
AB Serotonin (5-hydroxytryptamine; also called 5-HT) modifies cardiovascular activity by central as well as peripheral sites of action. When 5-HT is injected within the central nervous system, depending upon the dose and site of administration, either a pressor or a depressor effect is observed. Recent findings suggest that this depressor effect may be mediated by central "5-HT1-like" receptors, since certain compounds that exhibit a high affinity for the 5-**HT1A** binding site can reduce blood pressure by a central action in both hypertensive and normotensive animals. Peripherally, 5-HT elicits vasodilatation (both directly and indirectly via presynaptic sympathoinhibition and release of vasodilator substances from endothelium) or vasoconstriction (with associated amplification of noradrenaline response) of mainly "large" conductance arteries mediated by, respectively, "5-HT1-like" and 5-HT2 receptors. Of the various antagonists at 5-HT receptors, it is only ketanserin that effectively lowers arterial blood pressure. However, since it is unlikely that the very low concentrations of 5-HT in plasma exert a significant influence on the maintenance of peripheral vascular resistance, the blockade of 5-HT2 receptors by ketanserin does not seem to explain the reduction of blood pressure in hypertension. Indeed, apart from the undoubtedly potent 5-HT2 receptor blockade, ketanserin also has alpha 1-adrenoceptor antagonist, central **vasomotor** depressant, and "direct" vasodilator properties, which can explain its antihypertensive action.

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L25 ANSWER 1 OF 2 MEDLINE on STN
AN 96380517 MEDLINE
DN PubMed ID: 8788530
TI Electrophysiological, biochemical, neurohormonal and behavioural studies with WAY-100635, a potent, selective and silent 5-HT1A receptor antagonist.
AU Fletcher A; Forster E A; Bill D J; Brown G; Cliffe I A; Hartley J E; Jones D E; McLenachan A; Stanhope K J; Critchley D J; Childs K J; Middlefell V C; Lanfumey L; Corradetti R; Laporte A M; Gozlan H; Hamon M; Dourish C T
CS Department of Neuropharmacology, Wyeth Research, Ltd., Maidenhead, Berkshire, UK.
SO Behavioural brain research, (1996) 73 (1-2) 337-53.
Journal code: 8004872. ISSN: 0166-4328.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961204
AB Although considerable progress has been made in characterising the 5-HT1A receptor using agonists, partial agonists or non-selective antagonists, further studies of 5-HT1A receptor function have been hindered by the lack of highly selective antagonists. The term 'silent' antagonist has been used for such compounds in order to distinguish them unequivocally from several 5-HT1A receptor partial agonists which were initially designated 'antagonists'. In this report we provide a comprehensive **review** of the biochemical, pharmacological and behavioural properties of the first potent, selective and silent 5-HT1A receptor antagonist, WAY-100635 (N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-N-(2-pyridinyl)cyclohexanecarboxamide trihydrochloride). WAY-100635 had an IC50 (displacement of specific [3H]8-OH-DPAT binding to 5-HT1A receptors in the rat hippocampus) of 1.35 nM and was > 100-fold selective for the 5-HT1A site relative to a range of other CNS receptors. [3H]WAY-100635 was also characterised as the first 5-**HT1A antagonist** radioligand, displaying the same regional distribution of binding sites as [3H]8-OH-DPAT in rat brain. As would be expected for the binding of an antagonist to a G-protein-coupled receptor, the Bmax of [3H]WAY-100635 specific binding was consistently 50-60% greater than that of the agonist radioligand, [3H]8-OH-DPAT. Mn2+, but not guanine nucleotides, inhibited [3H]WAY-100635-specific binding. [3H]WAY-100635 was also shown to bind selectively to brain 5-HT1A receptors in vivo, following intravenous administration to mice. In vitro electrophysiological studies demonstrated that WAY-100635 had no 5-HT1A receptor agonist actions, but dose-dependently blocked the effects of agonists at both the postsynaptic 5-HT1A receptor in the CA1 region of the hippocampus, and the somatodendritic 5-HT1A receptor located on dorsal raphe 5-HT neurones. In vivo, WAY-100635 also dose-dependently blocked the ability of 8-OH-DPAT to inhibit the firing of dorsal raphe 5-HT neurones, and to induce the '5-HT syndrome', hypothermia, hyperphagia and to elevate plasma ACTH levels. In the mouse light/dark box anxiety model, WAY-100635 induced anxiolytic-like effects. WAY-100635 had no intrinsic effect on cognition in the delayed-matching-to-position model of short-term memory in the rat, but reversed the disruptive effects of 8-OH-DPAT on motor motivational performance. These data clearly demonstrate that WAY-100635 is the first potent, selective and silent 5-HT1A receptor antagonist. Furthermore, [3H]WAY-100635 is the first antagonist radioligand to become available for 5-HT1A receptor binding studies both in vitro and in vivo. The positive effects of WAY-100635 in an anxiety model also indicate that a postsynaptic 5-HT1A receptor antagonist action may contribute to the anxiolytic properties of 5-HT1A receptor partial agonists.

L25 ANSWER 2 OF 2 MEDLINE on STN
AN 91080619 MEDLINE
DN PubMed ID: 2259248
TI Application of brain microdialysis to study the pharmacology of the 5-HT1A autoreceptor.
AU Sharp T; Hjorth S
CS University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford U.K.
SO Journal of neuroscience methods, (1990 Sep) 34 (1-3) 83-90. Ref: 40
Journal code: 7905558. ISSN: 0165-0270.
CY Netherlands

106663533

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199101
ED Entered STN: 19910322
Last Updated on STN: 19910322
Entered Medline: 19910131

AB 5-Hydroxytryptamine (5-HT) receptors of the 5-HT1A subtype are localized on serotoninergic cells and dendrites in the raphe nuclei of the brain stem and are believed to regulate synaptic 5-HT release through an inhibitory influence on serotoninergic impulse flow. The effects of 5-HT1A agonists on 5-HT release can, therefore, only be detected by measurement of 5-HT release from intact serotoninergic neurones. Here we **review** the evidence that the microdialysis technique, when applied to the anaesthetized rat, is able to detect extracellular 5-HT in the brain which derives from serotoninergic neurones and changes in accordance with serotoninergic neuronal activity. We have observed that a range of 5-HT1A agonists, including 8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT), inhibit 5-HT release in hippocampus, most probably by acting on somatodendritic 5-HT1A autoreceptors in the dorsal raphe nucleus. The inhibitory action of 8-OH-DPAT and several other selective 5-HT1A receptor active drugs on 5-HT release is sensitive to pindolol, further supporting the idea that the 5-HT receptor being measured is of the 5-HT1 subtype. Two drugs, BMY 7378 and NAN-190, which show 5-**HT1A** **antagonist** properties in certain models, reduce 5-HT release indicating that they have mixed agonist/antagonist actions at the 5-HT1A receptor. Our data indicate that measurement of 5-HT release in rat brain using the microdialysis technique may be a useful method to probe the pharmacology of the 5-HT1A autoreceptor in vivo.

106663533

L28 ANSWER 1 OF 44 MEDLINE on STN
AN 2003541816 MEDLINE
DN PubMed ID: 14615704
TI [Interest of the use of pindolol in the treatment of depression: **review**].
Interet de l'utilisation du pindolol dans le traitement des depressions: revue de la litterature.
AU Brousse G; Schmitt A; Chereau I; Eschalier A; Dubray C; Llorca P-M
CS CMPB, Service de Psychiatrie Adulte, CHU, rue Montalembert, 63003 Clermont-Ferrand.
SO L'Encephale, (2003 Jul-Aug) 29 (4 Pt 1) 338-50. Ref: 50
Journal code: 7505643. ISSN: 0013-7006.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA French
FS Priority Journals
EM 200401
ED Entered STN: 20031119
Last Updated on STN: 20040115
Entered Medline: 20040114
AB The principal stakes of depression treatment are to accelerate and enhance the clinical effects of antidepressant drug. The onset of antidepressant action of Serotonin (5HT) selective reuptake inhibitors (SSRIs) was attributed in part to the decrease in firing activity of serotonin neurons produced by the activation of raphe **5HT1A** autoreceptors at the time of treatment initiation. Pindolol, an **antagonist** at somatodendritic pre-synaptic **5HT1A** receptors has been investigated as a potential accelerator or potentialisator of antidepressant response. Six open label studies and 12 controlled studies were identified for revue. The first open-label pilot study was conducted by Artigas et al. They showed promising results with pindolol, both in the acceleration of antidepressant response and in improving the efficacy of antidepressant. On the basis of these results five open-label studies were conducted. The open label studies suggest that pindolol accelerate the antidepressant response of serotoninergics therapeutics. The augmentation of antidepressant response was not clearly demonstrated by these studies particularly in the treatment of refractory depression. For example, Dinan et Scott that found the addition of pindolol in association with SSRI therapy had a poor efficacy. In the twelve controlled studies, 4 tried to underscore the shortening of the onset and the augmentation of efficacy of SSRI by pindolol [Berman et al., Maes et al., Perez et al., Tome et al.], 3 tried to underscore shortening of the onset [Bordet, Zanardi] and 3 tried to underscore the augmentation of efficacy [Maes et al., Moreno et al., Perez et al.]. One study tried to underscore the augmentation of efficacy of sleep deprivation by pindolol and another one the shortening of the onset of ECT. Six studies included depressive resistant patients. Three studies were carried out with fluoxetine, 1 with fluvoxamine, 3 with paroxetine, 1 with trazodone. Two -studies were investigated with several antidepressant treatments. The results of the studies indicate one acceleration of antidepressant response in 6 studies, one augmentation of efficacy in 5 studies. Two studies clearly demonstrate that pindolol may -augment and accelerate antidepressant response. Three studies did not confirm these observations. Several points can be examined. For pindolol: 3 authors have demonstrated that the effect of pindolol did not rely upon small antidepressant effect mediated by b-blockers properties, because anxiety was not predominantly improved by pindolol plus SSRI while depressive symptoms were clearly improved. On the basis of data issues from recent positron emission tomography (PET) studies, several authors suggested that the dose of pindolol used in most clinical trials (3 yen 2,5 mg day-1) might be insufficient to induce a substantial occupancy of 5-HTA receptors (Rabiner et al. It is possible that higher doses will show a more evident benefit. On the whole, pindolol seemed to be well tolerated. Adverse effects most commonly reported were increased irritability, insomnia and nausea. Pindolol had poor adverse effects in cardiovascular functions. The variation of the results of the controlled studies can be explained by different points: Firstly by difficulty to determine good criterion of resistance. The most simplistic definition of treatment resistance is the failure to achieve and sustain euthymia with adequate antidepressant treatment. Secondly by the fact that depressive patients who present antecedents of depressive illness seem to be worst responders to the association pindolol/serotoninergic antidepressant than patients suffering of first episode of depression. We observed one antecedent of depression in the group of resistant patients who were good responders to the

association pindolol/antidepressant therapy. We observed three anterior episodes of depression in negatives studies of the association pindolol/antidepressant therapy. Thirdly by the fact that the failure of the antidepressant treatment at the time of earlier (or actual) episode seems to be a criterion for less responsiveness to the association of this antidepressant treatment with pindolol. In fact, the open label studies who demonstrated efficacy of the association between pindolol and serotoninergic therapy in major resistant depression were realized with new antidepressant molecule for the episode. Other controlled trials could confirm these facts. Most of the studies failed to retrace clearly the historicity of depression, and it may be interesting in future investigations to analyze the response of the association -compared to the status of the patient with the antidepressant therapy. Further perspective could be envisaged especially in the utilization of pindolol for the treatment of pathologies which are usually treated with a serotoninergic antidepressant -therapy. For example, the **antagonist** 5HT(1A) Way 100635 was experimented with success in animals in order to augment the efficacy of clomipramine in the treatment of chronic pain. In other respects several psychopharmacogenetics studies could be investigated to examine, for instance, the role of the 5-HT transporter and its implication in the response to pindolol and antidepressant association. In summary, pindolol accele-rates, and in some cases enhances the clinical action of antidepressant drugs. It appears that this augmentation strategy has more limited effect on treatment resistant patient but there is experimental evidence for using higher doses in future augmentation trial.

=> d 2-10 bib abs

L28 ANSWER 2 OF 44 MEDLINE on STN
AN 2002663022 MEDLINE
DN PubMed ID: 12422559
TI [Mechanism of action of antidepressants and therapeutic perspectives]. Mecanisme d'action des antidepresseurs et perspectives therapeutiques.
AU Bourin M; David D J P; Jolliet P; Gardier A
CS Laboratoire de Neuropharmacologie Upres EAD MENRT, Institut de signalisation et d'innovation therapeutique (IFR75), Faculte de Pharmacie, Universite Paris-Sud, Chatenay-Malabry, France.. mbourin@sante.univ-nantes.fr
SO Therapie, (2002 Jul-Aug) 57 (4) 385-96. Ref: 51
Journal code: 0420544. ISSN: 0040-5957.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA French
FS Priority Journals
EM 200212
ED Entered STN: 20021109
Last Updated on STN: 20021217
Entered Medline: 20021210
AB Depression is an incapacitating disease which needs appropriate treatment. This article **reviews** the pharmacology of antidepressant drugs and the future perspectives of treating mood disorders such as depression. The foremost theory for explaining the biological basis of depression has been the monoamine hypothesis. Depression is due to a deficiency in one or other biogenic monoamines (serotonin, 5-HT; noradrenaline, NA; dopamine, DA). Antidepressant drugs are therefore classified according to their ability to improve monoaminergic transmission. Since this first theory, other explanations based on abnormal function of monoamine receptors or associated with impaired signalling pathways have been suggested. Notable progress has been accomplished in the treatment of major depressive disorders with new compounds recently discovered (selective serotonin reuptake inhibitors: SSRI; serotonin noradrenaline reuptake inhibitors: SNRI). Behavioural, electrophysiological and microdialysis studies have shown that serotonin (5-HT) receptors, mainly 5-**HT1A**, 5-HT1B and 5-HT2C sub-types, exert a key role in modulating antidepressant activity. Indirect activation of neurotransmitter receptors by antidepressants may also lead,' via increases in endogenous levels of serotonin in synapses in specific brain regions, to activation of various G proteins coupled to a receptor, signal of transduction, transcription factors and neurotrophic factors such as brain-derived neurotrophic factor (BDNF). Thus, depression may be considered as a transduction mechanism anomaly. This hypothesis needs to be clarified by molecular biology. Although antidepressants have improved

the therapeutic potential compared to tricyclics (TCA) in terms of reduced side effects, a number of problems still occur with these drugs. Clinical effects are not always observed until after this time has elapsed (4-6 weeks) and a substantial proportion of depressed patients show only partial or no response to antidepressants. Knowledge of the existence of links between neurotransmitter systems and the discovery of the most specific target, 5-HT receptors, should lead to improvements in antidepressant therapy. Developing drugs using innovative mechanisms such as directly acting on 5-HT receptors (5-**HT1A** agonists or 5-HT2 **antagonists**), would appear to be useful in the treatment of depression. The use of antidepressants in anxiety disorders such as obsessional compulsive disorders and even generalised anxiety, highlights the distinction between antidepressants and classic anxiolytics such as benzodiazepines, or even buspirone.

L28 ANSWER 3 OF 44 MEDLINE on STN
AN 2002639063 MEDLINE
DN PubMed ID: 12397861
TI Risperidone: **review** of its therapeutic utility in depression.
AU Myers J E; Thase M E
CS Janssen Pharmaceutical, Titusville, NJ, USA.
SO Psychopharmacology bulletin, (2001 Autumn) 35 (4) 109-29. Ref: 55
Journal code: 0101123. ISSN: 0048-5764.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20021026
Last Updated on STN: 20021211
Entered Medline: 20021113
AB There is extensive evidence to implicate dysregulation of noradrenergic, serotonergic, and dopaminergic neurotransmission in the pathophysiology of mood disorders. The receptor profile for risperidone, an atypical antipsychotic with demonstrated efficacy in schizophrenia, is consistent with possible antidepressant activity. Specifically, risperidone is a potent **antagonist** of central 5-HT2A receptors, addressing symptoms such as insomnia, agitation, and weight loss and may indirectly enhance 5-**HT1A**-mediated neurotransmission. A search of the worldwide medical literature published through December 2000 revealed 24 publications pertinent to the clinical use of risperidone in the treatment of patients with depressive symptomatology. In schizophrenia, in which depression is a common comorbid condition, the results of eight randomized, blinded, and controlled trials consistently demonstrated that treatment with risperidone significantly reduced scores on various measures of depressive symptoms. Moreover, these effects were distinct from improvements in negative and positive symptoms. Antidepressant effects also were observed in two large meta-analyses of trials in patients with schizophrenia or schizoaffective disorder. Observations from uncontrolled studies and case reports of risperidone therapy of other psychiatric disorders were similarly suggestive of antidepressant activity. Collectively, the evidence we present in this **review** indicates that risperidone's therapeutic benefits in psychiatric medicine extend beyond potent and effective antipsychotic activity and may include effectiveness in treating depression and related affective disorders. Systematic studies are now needed to evaluate the utility of concomitant therapy with an atypical antipsychotic in psychotic, bipolar, and treatment-resistant depressive syndromes.

L28 ANSWER 4 OF 44 MEDLINE on STN
AN 2002379219 MEDLINE
DN PubMed ID: 12101361
TI Primary neurotransmitters and regulatory substances onto vestibular nucleus neurons.
AU Sasa M; Takeshita S; Amano T; Kurisu K
CS Department of Pharamacology, Hiroshima University School of Medicine, Hiroshima, Japan.. masa@hiroshima-u.ac.jp
SO Uchu seibutsu kagaku, (2001 Dec) 15 (4) 371-4. Ref: 22
Journal code: 100972048. ISSN: 0914-9201.
Report No.: NASA-00027996.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)

106663533

LA English
FS Space Life Sciences
EM 200209
ED Entered STN: 20020720
Last Updated on STN: 20020928
Entered Medline: 20020927
AB This **review** article focused on the primary neurotransmitters involved in transmission from the otolith to the vestibular nucleus (VN), especially in relation to the neurotransmission to the VN neurons (gravity-sensitive neurons) activated by tilt stimulation. The medial vestibular nucleus (MVN) neurons were classified in 8 types (alpha-theta) according to the patterns in response to the clockwise and counterclockwise tilt-stimulations. The tilt-induced firing was inhibited by GDEE (a non-selective glutamate receptor **antagonist**) and/or atropine (a muscarinic receptor **antagonist**). Thus, glutamate and/or acetylcholine may serve as the primary neurotransmitters. This conclusion is supported by the previous findings that glutamate exists in the vestibular nerve and is released from the nerve besides the presence of glutamate receptor subtypes in the VN. In addition, acetylcholine induced atropine-reversible firing of MVN neurons, and the enzymes involved in acetylcholine synthesis/metabolism are also found in the VN. Furthermore, serotonin was found to inhibit the MVN neuronal activities via the 5-**HT1A** receptors. As such, the 5-**HT1A** agonist, tandospirone, may be effective in preventing and/or treating motion sickness and/or space sickness.

L28 ANSWER 5 OF 44 MEDLINE on STN
AN 2001295101 MEDLINE
DN PubMed ID: 11379796
TI The augmentation hypothesis for improvement of antidepressant therapy: is pindolol a suitable candidate for testing the ability of **5HT1A** receptor **antagonists** to enhance SSRI efficacy and onset latency?.
AU Kinney G G; Taber M T; Gribkoff V K
CS Bristol-Myers Squibb Pharmaceutical Research Institute, Neuroscience and Genitourinary Drug Discovery, Wallingford, CT 06492, USA.. kinneyg@bms.com
SO Molecular neurobiology, (2000 Jun) 21 (3) 137-52. Ref: 103
Journal code: 8900963. ISSN: 0893-7648.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200110
ED Entered STN: 20011022
Last Updated on STN: 20030118
Entered Medline: 20011018
AB The development of selective serotonin reuptake inhibitors (SSRIs) provided a major advancement in the treatment of depression. However, these drugs suffer from a variety of drawbacks, most notably a delay in the onset of efficacy. One hypothesis suggests that this delay in efficacy is due to a paradoxical decrease in serotonergic (5-HT) neuronal impulse flow and release, following activation of inhibitory presynaptic 5-**HT1A** autoreceptors, following acute administration of SSRIs. According to the hypothesis, efficacy is seen only when this impulse flow is restored following desensitization of 5-**HT1A** autoreceptors and coincident increases in postsynaptic 5-HT levels are achieved. Clinical proof of this principal has been suggested in studies that found a significant augmenting effect when the beta-adrenergic/5-**HT1A** receptor **antagonist**, pindolol, was coadministered with SSRI treatment. In this article, we **review** preclinical electrophysiological and microdialysis studies that have examined this desensitization hypothesis. We further discuss clinical studies that utilized pindolol as a test of this hypothesis in depressed patients and examine preclinical studies that challenge the notion that the beneficial effect of pindolol is due to functional antagonism of the 5-**HT1A** autoreceptors.

L28 ANSWER 6 OF 44 MEDLINE on STN
AN 2001154655 MEDLINE
DN PubMed ID: 11202445
TI Visualisation of serotonin-1A (5-HT1A) receptors in the central nervous system.
AU Passchier J; van Waarde A
CS PET Center, University Hospital Groningen, The Netherlands.

106663533

SO European journal of nuclear medicine, (2001 Jan) 28 (1) 113-29. Ref: 131
Journal code: 7606882. ISSN: 0340-6997.
CY Germany: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20030118
Entered Medline: 20010322
AB The 5-**HT1A** subtype of receptors for the neurotransmitter serotonin is predominantly located in the limbic forebrain and is involved in the modulation of emotion and the function of the hypothalamus. Since 5-**HT1A** receptors are implicated in the pathogenesis of anxiety, depression, hallucinogenic behaviour, motion sickness and eating disorders, they are an important target for drug therapy. Here, we **review** the radioligands which are available for visualisation and quantification of this important neuroreceptor in the human brain, using positron emission tomography (PET) or single-photon emission tomography (SPET). More than 20 compounds have been labelled with carbon-11 (half-life 20 min), fluorine-18 (half-life 109.8 min) or iodine-123 (half-life 13.2 h): structural analogues of the agonist, 8-OH-DPAT, structural analogues of the **antagonist**, WAY 100635, and apomorphines. The most successful radioligands thus far are [carbonyl-11C] WAY-100635 (WAY), [carbonyl-11C]desmethyl-WAY-100635 (DWAY), p-[18F]MPPF and [11C]robalzotan (NAD-299). The high-affinity ligands WAY and DWAY produce excellent images of 5-**HT1A** receptor distribution in the brain (even the raphe nuclei are visualised), but they cannot be distributed to remote facilities and they probably cannot be used to measure changes in endogenous serotonin. Binding of the moderate-affinity ligands MPPF and NAD-299 may be more sensitive to serotonin competition and MPPF can be distributed to PET centres within a flying distance of a few hours. Future research should be directed towards: (a) improvement of the metabolic stability in primates; (b) development of a fluorinated radioligand which can be produced in large quantities and (c) production of a radioiodinated or technetium-labelled ligand for SPET.

L28 ANSWER 7 OF 44 MEDLINE on STN
AN 2001128281 MEDLINE
DN PubMed ID: 11185947
TI Pindolol augmentation of antidepressants: a **review** and rationale.
AU Olver J S; Cryan J F; Burrows G D; Norman T R
CS Department of Psychiatry, University of Melbourne, Austin & Repatriation Medical Centre, Heidelberg, Victoria, Australia.
SO Australian and New Zealand journal of psychiatry, (2000 Feb) 34 (1) 71-9.
Ref: 43
Journal code: 0111052. ISSN: 0004-8674.
CY Australia
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301
AB OBJECTIVE: To critically **review** the literature on clinical trials in which pindolol, a **5HT1A** receptor **antagonist**, has been used to augment the effects of antidepressants in patients with depression and to examine the pharmacodynamics and pharmacokinetics that may underlie such augmentations. METHOD: The available literature from the previous 10 years relating to the clinical use of pindolol in combination with antidepressants was critically examined. This was placed in the context of its pharmacodynamic rationale, and evidence supporting its use was critically **reviewed**. RESULTS: A number of open-label and placebo-controlled, double-blind trials on patients with depression showed conflicting results as to the value of adding pindolol to various antidepressant regimens in reducing latency or in augmenting the antidepressant effect in treatment-resistant cases. While pre-clinical studies using electrophysiological and microdialysis techniques suggest utility in terms of increases in extracellular

concentration of 5-hydroxy-tryptamine (5HT) in serotonergic projection areas, few studies have examined the possibility of drug-drug interactions and subsequent elevated plasma levels of antidepressant. CONCLUSIONS: Pre-clinical studies suggest possible advantages of pindolol augmentation of antidepressant regimens and the achievement of faster acting antidepressants. The results of investigations in patients with depression have so far been conflicting. There exists the possibility of drug-drug interaction in pindolol/antidepressant augmentation strategies which remains to be examined.

L28 ANSWER 8 OF 44 MEDLINE on STN
AN 2000124621 MEDLINE
DN PubMed ID: 10659396
TI Antiemetics for cancer chemotherapy-induced nausea and vomiting. A **review** of agents in development.
AU Rizk A N; Hesketh P J
CS St Elizabeth's Medical Center, Boston, Massachusetts, USA.
SO Drugs in R&D, (1999 Oct) 2 (4) 229-35. Ref: 67
Journal code: 100883647. ISSN: 1174-5886.
CY New Zealand
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200002
ED Entered STN: 20000314
Last Updated on STN: 20000314
Entered Medline: 20000228
AB Significant progress has been made in recent years in developing more effective means of preventing nausea and vomiting induced by cancer chemotherapy. With appropriate application of currently available antiemetic regimens, the majority of patients with cancer who are receiving chemotherapy can anticipate experiencing no emesis during their treatment. Nevertheless, incompletely controlled emesis remains a problem for a significant percentage of patients. Persistent challenges include delayed emesis and emesis following high-dose chemotherapy regimens. The goal of complete prevention of emesis in all patients remains elusive. Therefore, there is a strong rationale for investigating new antiemetic approaches. New antiemetic agents currently under development target the neurotransmitters serotonin (5-hydroxytryptamine; 5-HT) and substance P. A number of new selective **antagonists** of serotonin 5-HT3 receptors are in clinical trials. Given the lack of clinically significant differences between the available 5-HT3 receptor **antagonists**, it appears unlikely that any of these new agents will have substantial advantages over currently approved agents. Several other serotonin receptors have been targeted including the 5-HT4, 5-**HT1A** and 5-HT2A receptors. Of these approaches, only agonism of the 5-**HT1A** receptor has produced an agent that has proceeded into clinical testing. The most exciting new class of antiemetics currently under development focuses on antagonism of the effects of the neurotransmitter substance P. Results of early clinical trials with tachykinin neurokinin NK1 receptor **antagonists** demonstrate enhanced control of acute emesis with their addition to currently available agents and promising activity in controlling delayed emesis. Available evidence would strongly suggest that this class of agents will represent the next important advance in efforts to control nausea and vomiting induced by chemotherapy.

L28 ANSWER 9 OF 44 MEDLINE on STN
AN 2000007073 MEDLINE
DN PubMed ID: 10541060
TI The conditioned avoidance response test re-evaluated: is it a sensitive test for the detection of potentially atypical antipsychotics?.
AU Wadenberg M L; Hicks P B
CS Department of Psychiatry, Scott & White Clinic, Temple, TX 75608, USA..
wadenbergm@cs.clarke-inst.on.ca
SO Neuroscience and biobehavioral reviews, (1999) 23 (6) 851-62. Ref: 122
Journal code: 7806090. ISSN: 0149-7634.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199912

106663533

ED Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991213

AB The present **review** discusses the history and paradigm of the conditioned avoidance response (CAR) in rats for the detection of potential antipsychotic activity of drugs. In addition, the role of dopamine (DA) D2, serotonin (5-HT)2A/2C, alpha1, 5-**HT1A**, DA D4, muscarinic and glutamate receptors in the suppression of CAR induced by various classes of drugs is evaluated. Finally, data investigating brain sites of action for the mediation of CAR behavior is discussed. It is concluded that the CAR test, originally found to be sensitive for the detection of antipsychotic drugs with high affinity as **antagonists** for brain dopamine receptors, is also sensitive for the detection of potentially antipsychotic compounds acting primarily via neurotransmitter receptors other than the DA D2 receptor. Furthermore, the **review** confirms the importance of the nucleus accumbens(shell) in the mediation of effects on CAR produced by traditional, as well as atypical antipsychotic drugs.

L28 ANSWER 10 OF 44 MEDLINE on STN
AN 1999414347 MEDLINE
DN PubMed ID: 10482904
TI The recombinant 5-HT1A receptor: G protein coupling and signalling pathways.
AU Raymond J R; Mukhin Y V; Gettys T W; Garnovskaya M N
CS Division of Nephrology, Department of Medicine, Medical University of South Carolina and the Ralph H. Johnson Veterans Affairs Medical Center, Charleston, South Carolina 29425, USA.. raymondj@musc.edu
NC DK52448 (NIDDK)
DK53891 (NIDDK)
SO British journal of pharmacology, (1999 Aug) 127 (8) 1751-64. Ref: 160
Journal code: 7502536. ISSN: 0007-1188.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA English
FS Priority Journals
EM 199910
ED Entered STN: 19991101
Last Updated on STN: 20030118
Entered Medline: 19991021

AB The 5-hydroxytryptamine 5-**HT1A** receptor was one of the first G protein coupled receptors whose cDNA and gene were isolated by molecular cloning methods. Transfection of the cDNA of this receptor into cells previously bearing no 5-HT receptors has resulted in the acquisition of large amounts of information regarding potential signal transduction pathways linked to the receptor, correlations of receptor structure to its various functions, and pharmacological properties of the receptor. Transfection studies with the 5-**HT1A** receptor have generated critical new information that might otherwise have been elusive. This information notably includes the discovery of unsuspected novel signalling linkages, the elucidation of the mechanisms of receptor desensitization, the refinement of models of the receptor pharmacophore, and the development of silent receptor **antagonists**, among others. The current **review** summarizes the most important studies of the recombinant 5-**HT1A** receptor in the decade since the identification of its cDNA.

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L28 ANSWER 11 OF 44 MEDLINE on STN
AN 1999171904 MEDLINE
DN PubMed ID: 10073896
TI Effects of centrally administered anxiolytic compounds in animal models of anxiety.
AU Menard J; Treit D
CS Department of Psychology, University of Alberta, Edmonton, Canada.
SO Neuroscience and biobehavioral reviews, (1999 Mar) 23 (4) 591-613. Ref: 156
Journal code: 7806090. ISSN: 0149-7634.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)

106663533

LA English
FS Priority Journals
EM 199903
ED Entered STN: 19990413
Last Updated on STN: 19990413
Entered Medline: 19990326
AB The effect of intra-cerebrally infused compounds in animal models of anxiety were **reviewed**. A large body of evidence suggested that benzodiazepine agonists in different brain regions--including areas of the raphe, hypothalamus, periaqueductal gray, septum, hippocampus, and amygdala--produce reasonably consistent anxiolytic effects in a variety of animal models. However, evidence regarding the effects on anxiety of 5-**HT1A** agonists, 5-HT2 compounds, and 5-HT3 **antagonists** was somewhat less extensive, both anatomically and behaviourally, and more complex. For example, establishing receptor specificity for 5-HT ligand effects was often complicated by the lack of 'silent' and/or selective **antagonists**. Neuropeptides had significant effects on anxiety, but these were shown in a smaller number of animal models and in a limited number of brain regions. Regardless of the compounds tested, however, there seemed to be a surprising number of double dissociations (brain site by behavioural test). In fact in some instances, different fear reactions appeared to be controlled by distinct receptor subpopulations within particular parts of the limbic system. These results suggest that the neural control of anxiety might be analogous in organization to sensorimotor systems, i.e., anxiety is controlled by complex systems of multiple, distributed, parallel pathways.

L28 ANSWER 12 OF 44 MEDLINE on STN
AN 1999131645 MEDLINE
DN PubMed ID: 9934946
TI Effects of SSRIs on sexual function: a critical **review**.
CM Comment in: J Clin Psychopharmacol. 2001 Apr;21(2):241-2. PubMed ID: 11270925
AU Rosen R C; Lane R M; Menza M
CS Department of Psychiatry, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, Piscataway 08854, USA.
SO Journal of clinical psychopharmacology, (1999 Feb) 19 (1) 67-85. Ref: 255
Journal code: 8109496. ISSN: 0271-0749.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199904
ED Entered STN: 19990420
Last Updated on STN: 20020219
Entered Medline: 19990407
AB Sexual problems are highly prevalent in both men and women and are affected by, among other factors, mood state, interpersonal functioning, and psychotropic medications. The incidence of antidepressant-induced sexual dysfunction is difficult to estimate because of the potentially confounding effects of the illness itself, social and interpersonal comorbidities, medication effects, and design and assessment problems in most studies. Estimates of sexual dysfunction vary from a small percentage to more than 80%. This article **reviews** current evidence regarding sexual side effects of selective serotonin reuptake inhibitors (SSRIs). Among the sexual side effects most commonly associated with SSRIs are delayed ejaculation and absent or delayed orgasm. Sexual desire (libido) and arousal difficulties are also frequently reported, although the specific association of these disorders to SSRI use has not been consistently shown. The effects of SSRIs on sexual functioning seem strongly dose-related and may vary among the group according to serotonin and dopamine reuptake mechanisms, induction of prolactin release, anticholinergic effects, inhibition of nitric oxide synthetase, and propensity for accumulation over time. A variety of strategies have been reported in the management of SSRI-induced sexual dysfunction, including waiting for tolerance to develop, dosage reduction, drug holidays, substitution of another antidepressant drug, and various augmentation strategies with 5-hydroxytryptamine-2 (5-HT2), 5-HT3, and alpha2 adrenergic receptor **antagonists**, 5-**HT1A** and dopamine receptor agonists, and phosphodiesterase (PDE5) enzyme inhibitors. Sexual side effects of SSRIs should not be viewed as entirely negative; some studies have shown improved control of premature ejaculation in men. The impacts of sexual side effects of SSRIs on treatment compliance and on patients' quality of life are important

clinical considerations.

L28 ANSWER 13 OF 44 MEDLINE on STN
AN 1999079780 MEDLINE
DN PubMed ID: 9864076
TI Involvement of serotonin and dopamine in the mechanism of action of novel antidepressant drugs: a **review**.
AU Bonhomme N; Esposito E
CS Istituto di Ricerche Farmacologiche Mario Negri, Consorzio Mario Negri Sud, Santa Maria Imbaro (Chieti), Italy.
SO Journal of clinical psychopharmacology, (1998 Dec) 18 (6) 447-54. Ref: 103
Journal code: 8109496. ISSN: 0271-0749.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199902
ED Entered STN: 19990301
Last Updated on STN: 19990301
Entered Medline: 19990218
AB Several hypotheses regarding the physiopathology of major depression exist. Attention has been focused on cerebral monoaminergic systems, the dysfunction of which is thought to underlie various aspects of depressive symptomatology. There is extensive literature describing the involvement of serotonergic and dopaminergic systems in the mechanism of action of antidepressant drugs. However, a unitary analysis of the data in terms of interaction between different monoaminergic systems is still lacking. In this article, studies reporting the biochemical, behavioral, and clinical effects of tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), selective blockers of presynaptic dopamine (DA) receptors, and **antagonists** of serotonin-2 (5-hydroxytryptamine-2 [5-HT2]) receptors were **reviewed**. Analysis of the current literature indicates that long-term treatment with antidepressants causes adaptive changes of the serotonergic and dopaminergic systems. In particular, long-term administration of TCAs enhances the responsiveness of postsynaptic serotonin receptors to iontophoretically applied serotonin and potentiates the behavioral responses to both direct and indirect dopaminergic agonists. Repeated administration of SSRIs and MAOIs increases serotonergic transmission by desensitizing the inhibitory 5-**HT1A** somatodendritic and terminal 5-HT1B/1D autoreceptors. Selective blockers of DA autoreceptors exert their antidepressant effect by enhancing DA release. A similar mechanism of action could be hypothesized for 5-HT2 receptor **antagonists**. There is general agreement that the clinical effect of antidepressant drugs, which becomes evident only after long-term treatment, is caused by their ability to induce adaptive changes of the monoaminergic systems. Increases in both serotonergic and dopaminergic function have been consistently found after long-term treatment with various classes of antidepressant drugs. Recent studies have focused on the functional interaction between the serotonergic and dopaminergic systems to explain the mechanism of the antidepressant action of SSRIs and 5-HT2 **antagonists**.

L28 ANSWER 14 OF 44 MEDLINE on STN
AN 1999078606 MEDLINE
DN PubMed ID: 9861613
TI Ventrolateral medullary control of cardiovascular activity during muscle contraction.
AU Ally A
CS Department of Pharmacology, University of New England, College of Osteopathic Medicine, Biddeford, ME 04005, USA.. aally@mail-box.une.edu
SO Neuroscience and biobehavioral reviews, (1998) 23 (1) 65-86. Ref: 206
Journal code: 7806090. ISSN: 0149-7634.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199903
ED Entered STN: 19990326
Last Updated on STN: 19990326
Entered Medline: 19990315

106663533

AB An overview of the role of ventrolateral medulla (VLM) in regulation of cardiovascular activity is presented. A summary of VLM anatomy and its functional relation to other areas in the central nervous system is described. Over the past few years, various studies have investigated the VLM and its involvement in cardiovascular regulation during static muscle contraction, a type of static exercise as seen, for example, during knee extension or hand-grip exercise. Understanding the neural mechanisms that are responsible for regulation of cardiovascular activity during static muscle contraction is of particular interest since it helps understand circulatory adjustments in response to an increase in physical activity. This **review** surveys the role of several receptors and neurotransmitters in the VLM that are associated with changes in mean arterial pressure and heart rate during static muscle contraction in anesthetized animals. Possible mechanisms in the VLM that modulate cardiovascular changes during static muscle contraction are summarized and discussed. Localized administration of an excitatory amino-acid **antagonist** into the rostral portion of the VLM (RVLM) attenuates increases in blood pressure and heart rate during static muscle contraction, whereas its administration into the caudal part of the VLM (CVLM) augments these responses. Opioid or 5-**HT1A** receptor stimulation in the RVLM, but not in the CVLM, attenuates cardiovascular responses to muscle contraction. Furthermore, intravenous, intracerebroventricular or intracisternal injection of an alpha 2-adrenoceptor agonist or a cholinesterase inhibitor attenuates increases in blood pressure and heart rate during static muscle contraction. Finally, the possible involvement of endogenous neurotransmitters in the RVLM and the CVLM associated with cardiovascular responses during static muscle contraction is discussed. An overview of the role of the VLM in the overall cardiovascular control network in the brain is presented and critically **reviewed**.

L28 ANSWER 15 OF 44 MEDLINE on STN
AN 1998246243 MEDLINE
DN PubMed ID: 9586831
TI Cholinergic/serotonergic interactions in hypothermia: implications for rat models of depression.
AU Overstreet D H; Daws L C; Schiller G D; Orbach J; Janowsky D S
CS Skipper Bowles Center for Alcohol Studies and the Department of Psychiatry, University of North Carolina School of Medicine, Chapel Hill 27599-7178, USA.
SO Pharmacology, biochemistry, and behavior, (1998 Apr) 59 (4) 777-85. Journal code: 0367050. ISSN: 0091-3057.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199806
ED Entered STN: 19980713
Last Updated on STN: 19980713
Entered Medline: 19980626
AB This article **reviews** published reports and presents new evidence that support a number of commonalties between lines of rats selectively bred for differences in cholinergic (muscarinic) and serotonergic (5-**HT1A**) sensitivity. The Flinders Sensitive Line (FSL) rat, a genetic animal model of depression derived for cholinergic supersensitivity, is more sensitive to both cholinergic and serotonergic agonists, and exhibits exaggerated immobility in the forced swim test relative to the control, Flinders Resistant Line (FRL), rat. Similar exaggerated responses are seen in a line of rats recently selected for increased sensitivity to the 5-**HT1A** agonist, 8-OH-DPAT (High DPAT Sensitive--HDS), relative to lines selectively bred for either low (Low DPAT Sensitive--LDS) or random (Random DPAT Sensitive--RDS) sensitivity to 8-OH-DPAT. For both the FSL and HDS rats, their exaggerated immobility in the forced swim test is reduced following chronic treatment with antidepressants. The present studies examined further the interaction between cholinergic and serotonergic systems in the above lines. Supersensitive hypothermic responses to 8-OH-DPAT were observed very early (postnatal day 18) in FSL rats, suggesting that both muscarinic and serotonergic supersensitivity are inherent characteristics of these rats. Scopolamine, a muscarinic **antagonist**, completely blocked the hypothermic effects of the muscarinic agonist oxotremorine in FSL and FRL rats, but had no effect on the hypothermic responses to 8-OH-DPAT, suggesting an independence of muscarinic and 5-**HT1A** systems. On the other hand, genetic selection of genetically heterogeneous rats for differential hypothermic responses to the muscarinic agonist oxotremorine were accompanied by differential

hypothermic responses to 8-OH-DPAT, suggesting an interaction between muscarinic and 5-**HT1A** systems. Overall, these studies argue for an inherent interaction between muscarinic and 5-**HT1A** systems, which probably occurs beyond the postsynaptic receptors, possibly at the level of G proteins.